VOLUME 41 NUMBER 1

ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY

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JANUARY 1940

PUBLISHED BY THE AMERICAN MEDICAL ASSOCIATION, 535 [illegible]
CHICAGO, ILLINOIS. ANNUAL SUBSCRIPTION [illegible]

Entered Oct. 25, 1917, at the Postoffice at Chicago, Ill., under the Act of Congress of March 3, 1879

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Archives of Dermatology and Syphilology

VOLUME 41 JANUARY 1940 NUMBER 1

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ROENTGEN DOSAGE IN DERMATOLOGY EXPRESSED IN INTERNATIONAL ROENTGENS

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AND

ANTHONY C. CIPOLLARO, M.D.

NEW YORK

In a previous communication before this section we [1] stated that the erythema dose for unfiltered radiation with 100 kilovolts was 300 roentgens. In the present communication we shall give the roentgen equivalents experimentally obtained for erythema doses for filtered radiations commonly used in dermatology. The majority of roentgenologists use between 550 and 700 r as the erythema dose with filtered high voltage radiations. The German roentgenologists, according to Küstner,[2] use 551 r plus or minus 15 per cent for the erythema dose of filtered radiations. At the Cleveland Clinic 600 r is required to produce erythema with heavily filtered roentgen rays. Pfahler [3] gave 650 and 700 r for an erythema, while Failla [4] stated that 600 r was required to produce redness with heavily filtered radiations. With 4 mm. of aluminum and 127 kilovolts, Widmann [5] used 600 r as the erythema dose. The different investigators were more in agreement in regard to the erythema dose of filtered radiation in terms of roentgens than for the erythema dose of unfiltered radiation.

Dermatologists have radiologic problems peculiar to their specialty. For the most part, even the thick and the deep lesions which the

From the Skin and Cancer Unit, New York Post-Graduate Medical School and Hospital, Columbia University.

Read before the Section on Dermatology and Syphilology at the Ninetieth Annual Session of the American Medical Association, St. Louis, May 17, 1939.

1. MacKee, G. M., and Cipollaro, A. C.: The Roentgen Unit in Dermatology, Arch. Dermat. & Syph. **30**:761 (Dec.) 1934.

2. Küstner, H.: Wie viel R-Einheiten entspricht die HED? Strahlentherapie **26**:120, 1927.

3. Pfahler, G. E., in discussion on Newell, R. R.: Shall We Record and Report All X-Ray Dosages in Roentgens? Radiology **21**:216 (Sept.) 1933.

4. Failla, G., in discussion on Newell, R. R.: Shall We Record and Report All X-Ray Dosages in Roentgens? Radiology **21**:216 (Sept.) 1933.

5. Widmann, B. P.: Unfiltered Roentgen Rays for Cancers of Wide and Deep Involvement, Am. J. Roentgenol. **28**:526 (Oct.) 1932.

dermatologists treat are superficial when compared with those treated by roentgen therapeutists. The thickness is seldom over 4 cm. Experience has shown that for dermatologic therapy with filtered roentgen radiation 137 kilovolts and from 0.5 to 3 mm. of aluminum are most desirable. There is a scarcity of material in the literature dealing with these particular factors.

THE ERYTHEMA DOSE

To ascertain the erythema dose in terms of roentgens, we selected 34 subjects at random for our studies. Fourteen of these were women and 20 were men. The ages varied from 14 to 36 years. Of these 34 subjects 21 were brunets, 9 were blonds, 2 had medium complexions, 1 had red hair and for 1 the kind of complexion was not recorded. Areas of skin 1 inch (2.5 cm.) square were exposed to various intensities of radiation. Four or five areas were exposed on each person. These were on the flexor surface of the forearm or on the inner surface of the thigh. From 270 to 720 r (measured in air) was administered to each area. The kilovoltage was 137, the milliamperage 5 and the skin-focal distance 10 inches (25 cm.). The filters used were 0.5, 1 and 3 mm. of aluminum. A mechanical rectifying machine and a broad focus Collidge tube were used in all cases. The intensity of radiation for 0.5 mm. aluminum was 120 r per minute; for 1 mm. it was 112.5 r per minute, and for 3 mm. it was 68.75 r per minute. The ionization instrument which we used was the Victoreen r meter.

The patients were divided into three groups: In group 1 were 10 on whom tests were made with a filter of 0.5 mm. aluminum; in group 2 were 10 on whom tests were made with a filter of 1 mm. aluminum, and in group 3 were 14 on whom tests were made with a filter of 3 mm. aluminum. In group 1 erythema was noted in the majority of subjects with 400 r. In some blonds erythema was noted with as little as 350 r, and in brunets it was difficult to determine definite erythema with even 500 r. Each test area received from 300 to 540 r. We therefore compromised on 400 r as the erythema dose for radiation filtered through 0.5 mm. aluminum.

The second group was tested with 1 mm. aluminum. Five areas were selected in each subject, and to each a dose of from 400 to 720 r was administered. Erythema was noted in the majority of the subjects with 450 r. In some areas, faint redness was discerned with 400 r. Some areas receiving as much as 600 r showed only pigmentation. In some cases it was difficult to distinguish erythema from pigmentation. As a result of these observations we adopted 450 r arbitrarily as the erythema dose for radiation filtered through 1 mm. aluminum.

We tested four or five areas on each subject in group 3 with doses varying from 270 to 648 r. No reaction (neither pigmentation nor

erythema) was noted in areas exposed to less than 300 r. Pigmentation preceded erythema in practically all cases. Pigmentation was noted in four to seven days and erythema was observed in from ten to fourteen days. In the majority of the tested subjects erythema was observed with 500 to 600 r. Among these it was particularly difficult to distinguish erythema from pigmentation. As a result of these observations we adopted 550 r arbitrarily as the erythema dose for radiation filtered through 3 mm. aluminum.

The cutaneous changes noted in the group tested with filtered radiation were different from those noted in the group tested with unfiltered radiation. When we carried out our studies with unfiltered roentgen rays, the erythema provoked by the radiation was easily recognized. With filtered radiation, some difficulties were encountered. The ery-

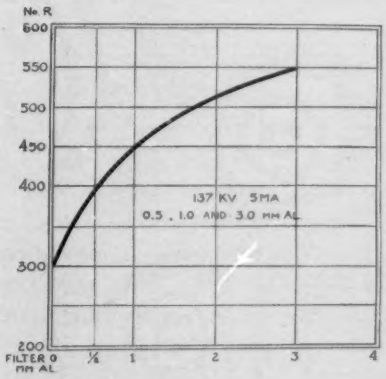

Fig. 1.—Curve to illustrate the relation of roentgens and erythema doses for roentgen ray qualities used in dermatology.

Relation Between Roentgens and Erythema Doses for Roentgen Ray Qualities Ordinarily Used in Dermatology

Kilovolts	Filter, Millimeters of Aluminum	Number Roentgens for Erythema	Intensity, Roentgens per Minute	Half Value Layer in Millimeters of Aluminum	Effective Wavelength
10 (Grenz)	0	200 to 300	150	0.02	1.75
60	0	300	100	0.8	0.27
80	0	300	100	1.0	0.264
90	0	300	100	1.1	0.260
100	0	300	100	1.3	0.253
115	0	300	100	1.9	0.240
137	0.5	400	120	2.7	0.228
137	1.0	450	112.5	3.0	0.224
137	3.0	550	68.75	4.2	0.213

thema was not easily observed. At first the skin would show a peculiar brownish color with a tinge of redness. When the dose was increased, this redness was more pronounced. With filtered radiation there was a

delay in the appearance of the erythema. It appeared in ten to fourteen days after treatment. As the thickness of the filter was increased, it was necessary to administer more roentgens to obtain erythema. The relation of the number of roentgens delivered per unit of time remained unchanged. No visible difference could be seen in the erythema produced by a "threshold dose" and that produced by a larger dose. The same difference was noted when the dose administered produced only pigmentation and was too small to cause erythema. In blonds the erythema was detected more easily than in brunets. In persons with dark complexions roentgen rays provoked a more decided pigmentary reaction. The cutaneous effects following exposure to filtered roentgen rays persisted from six weeks to several months. In all cases the reaction gradually subsided. Observation of some of these subjects several years later did not reveal radiation sequelae in the tested areas.

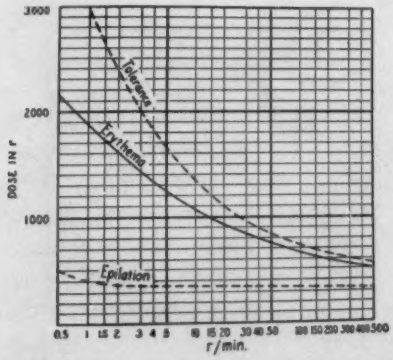

Fig. 2.—Relation of rate of administration of radiation to epilation, erythema and tolerance doses (Holthusen, H., and Braun, R.: Grundlagen und Praxis der Röntgenstrahlendosierung: Dosismessung und Dosisfestsetzung, Leipzig, Georg Thieme, 1933).

The half value layer in millimeters of aluminum for 137 kilovolts and 0.5 mm. aluminum was 2.7; for 1 mm. aluminum it was 3.0, and for 3 mm. aluminum it was 4.2. It is generally accepted that the erythema dose varies with the quality of the radiation used. Our experimental results conform with those quoted at the beginning of this paper even though the voltages we used did not exceed 137 kilovolts.

The erythema dose varies with the quality of the radiation and with the filtration. It also varies with the rate of administration of the dose. Holthusen and Braun [6] have illustrated the time-intensity factors of roentgen irradiation in a chart (fig. 2). For a given quality of radia-

6. Holthusen, H., and Braun, R.: Grundlagen und Praxis der Röntgenstrahlendosierung, Leipzig, Georg Thieme, 1933.

tion, they show that erythema is produced with 500 r if the total dose is delivered in one minute. If the total dose is delivered at the rate of 5 r per minute, then 1250 is required to produce erythema.

EPILATING DOSE

The epilating dose for unfiltered radiation is 300 r. For filtered radiation it is about the same. The chart by Holthusen and Braun contains a curve for the epilating dose. It is about 350 r. Epilation occurs after this amount of radiation is administered, regardless of whether it is applied slowly, at the rate of 5 r per minute, or rapidly, at the rate of 500 r per minute. It is interesting to note also that the epilating dose does not vary with either the quality of radiation (provided it is sufficiently penetrating to affect the hair papillae) or with the filtration.

ROUTINE FILTRATION

Dermatologists employ filtered radiation for the treatment of cutaneous neoplasms, keloids and other thick or deeply seated lesions. It is the belief of some roentgenologists that filtered radiation is safer because it does not produce the intense superficial reaction caused by unfiltered softer radiation. The reaction has been found to be about the same if the intensity, the total dose and the portals are the same. The danger may be greater with filtered than with unfiltered radiation because with soft roentgen rays the reaction affects chiefly the superficial tissues, while with hard radiation the deeper tissues are injured. During the past three years we have used filtered radiation in the treatment of several hundred patients with dermatoses. Our impression is that the results were no better than those obtained with unfiltered radiation. Also it is doubtful that filtered radiation is any safer than unfiltered radiation. In the final analysis, the size and depth of the lesions to be treated should decide the quality of the radiation. Most modern shock-proof apparatus will contain inherent filters equivalent to 0.5 to 1 mm. aluminum.

RADIATION QUALITY

The quality of a roentgen ray beam is best measured in actual practice by means of the half value layer, which has been repeatedly advocated as a preferential quality measure.[7] This method has become the international standard. Formerly photometric methods were used to determine the half value layer of a roentgen ray beam. Now standard

7. Meyer, W. H., and Glasser, O.: Erythema Doses in Absolute Units, Radiology **6**:320 (April) 1926. Meyer, W. H., and Braestrup, C. B.: Quality Determination of the Roentgen Rays, ibid. **11**:72 (July) 1928. Meyer, W. H.: The Co-Relation of Physical and Clinical Data in Radiation Therapy, ibid. **32**: 23 (Jan.) 1939.

roentgen meters are used for this purpose. Other means of measuring ray quality are by spectroscopic examination, by measurement of the spark gap and by the use of the following formula, which holds true only for a homogeneous roentgen ray beam:

$$\text{Minimum wavelength (in angstrom units)} = \frac{12.356}{\text{kilovolts}}$$

The half value layer may be defined as the thickness of any specified metal, usually copper or aluminum, which reduces the intensity of the incident beam to one half its value. The half value layer in aluminum of a specified roentgen ray beam may be obtained by measuring the amount of absorption in successive layers of the measured metal with an iontoquantimeter. These absorbed quantities are calculated in percentage, and the figures are plotted on ordinary graph paper or on logarithmic ruled paper. The percentages are plotted along the vertical and the thicknesses of the aluminum along the horizontal. The resultant curve thus obtained is called an "absorption curve." The thickness of the aluminum required to reduce the incident beam by 50 per cent is read directly from the curve.

GRENZ RAYS

At the present time instruments of sufficient accuracy to measure roentgen rays of low voltage (6 to 12 kilovolts) are not available. Therefore it is not possible to state with any degree of accuracy the number of roentgens required to produce erythema. We have personally experimented with two commercial grenz ray chambers and with three of our own make. The results have been inconstant. Since the Bureau of Standards does not calibrate grenz ray chambers, we have been handicapped in our endeavor to learn definitely the erythema dose for these supersoft roentgen rays. We therefore have to depend largely on skin effects (the erythema dose) and electric factors for measurements of doses. There are obvious limitations to this method. If we were to estimate the number of roentgens required to produce erythema with 10 kilovolts, we would say that it was no higher then 300 r. Perhaps 200 r would be nearer to the correct value. Glasser and Portmann [8] estimated the erythema dose for grenz rays (10 kilovolts) to be 250 r. Our results confirm their observations. We can give the exact figure only after we obtain an accurate measuring instrument.

Areas treated with 300 r showed decided erythema within forty-eight hours. After about one week pigmentation ensued and after several months this disappeared. In some cases telangiectasis, depigmentation, alopecia and atrophy developed. We have never observed,

8. Glasser, O., and Portmann, U. V.: The Physical and Clinical Foundations of Oversoft Roentgen-Ray (Grenz-Ray) Therapy, Am. J. Roentgenol. **19**:442-452 (May) 1928.

even after large doses administered over ten years ago, keratoses, ulceration or roentgen ray cancer following treatment with grenz rays.

For certain superficial lesions, treatment with supersoft roentgen rays is the method of choice. However, it is our opinion, based on many years of clinical observation and experimental studies, that this soft radiation is not superior to the beta rays or the soft gamma rays of radium or to the unfiltered low voltage roentgen rays in the treatment of ordinary dermatoses. Much clinical and experimental work remains to be done with radiations below 15 kilovolts.

CONCLUSIONS

1. The erythema dose for filtered radiation with 137 kilovolts and with 0.5 mm. aluminum is 400 r, with 1 mm. aluminum it is 450 r, and with 3 mm. aluminum it is 550 r.

2. The epilating dose is between 300 and 350 r and is independent of quality, filtration or intensity (roentgens per minute).

3. Filtration neither improves therapeutic results nor prevents radiation sequelae.

4. The half value layer is the practical and preferred method for measuring the quality of a roentgen ray beam.

5. Reliable grenz ray chambers are not available.

6. We estimate that the erythema dose with grenz rays is between 200 and 300 r. The therapeutic results are no better with grenz rays than with roentgen rays ordinarily used in dermatology. Radiodermatitis can be caused by grenz rays.

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ABSTRACT OF DISCUSSION

DR. GEORGE C. ANDREWS, New York: I was much interested in the paper of Drs. MacKee and Cipollaro, particularly in measuring the numbers of roentgens per erythema dose with filtrations of 1 mm. and 2 mm. of aluminum.

It is about five years since Dr. Braestrup and I presented a paper here on a similar subject. We discussed the number of roentgens per erythema dose with unfiltered radiation and with radiation filtered through 3 mm. of aluminum. At that time we stated 550 r was necessary for an erythema dose with 3 mm. of aluminum.

We also at that time said that 400 r was necessary for the erythema dose with unfiltered radiation. The number of roentgens for an erythema dose with unfiltered radiation is subject to a good many influences, as Dr. Cipollaro has stated. We worked with radiation from the mechanically rectified machines, and that radiation is in general a good deal harder than that obtained from the valve tube rectified machines such as Drs. MacKee and Cipollaro, I believe, used. For that reason, it takes a larger number of roentgens to produce erythema with radiation from

mechanically rectified machines than from machines with valve tube rectification. Of course, the number of roentgens for an erythema dose is influenced by many other factors, including the size of the area treated, the time element, the number of roentgens per minute and the quality of the radiation. For that reason I disagree with the statement that the figures reported in this paper are applicable to both types of machines. I don't think that they are.

Dr. Belisario of Sydney, Australia, wrote me a few days ago stating that he had been in this country, in London and in various places in Europe inquiring into the number of roentgens necessary for an erythema dose. He has been interested in that subject and was trying to get some figures and write a paper about it. He wrote, after inquiring in various places, that 400 r was what he thought was an erythema dose. So there is a little inconsistency in these results of 300 r and 400 r, which may seem considerable, but really is not so much when one considers the various discrepancies, difficulties and errors in the estimation of the dose, particularly when different equipment is used.

Dr. Harry R. Foerster, Milwaukee: Those who have witnessed or participated in the evolution of roentgen ray therapy and standardization of dosage probably appreciate the value of this contribution more fully than the younger dermatologists who are inclined to accept without question the dosage standards previously established. As a group, dermatologists are inclined to leave to others outside their specialty these important technical problems. It is gratifying, therefore, to find younger men like Drs. Cipollaro and Andrews carrying on the pioneer work of Drs. MacKee, Pusey and others.

Though most dermatologists use unfiltered roentgen rays, it is important to understand the technical differences involved in the use of filtered radiation. I believe the understanding of this work would be clearer if the fact were recognized that all roentgen ray therapy is actually filtered radiation therapy, for the glass wall of the air-cooled vacuum Coolidge tube presents a filter equivalent to approximately 0.5 mm. of aluminum. This is the filtration reported by Dr. Cipollaro for the modern shock-proof tube, so that the increasing use of the latter need not alter one's conception of doses for so-called unfiltered radiation.

The difference between the erythema effect of unfiltered radiation and radiation filtered through metal is chiefly a biologic one. The soft, or long wave, radiation that predominates in unfiltered radiation is largely absorbed by the first 2 or 3 mm. of skin. This acts chiefly on the capillaries of the papillae. A relatively smaller percentage of filtered radiation is absorbed in the superficial tissues, and the erythema from such radiation is in part due to effects on deeper and larger vessels. In the latter instance the erythema is less sharply defined, and larger quantities of radiation may be introduced without marked intensification of the visible erythema effect.

The authors have directed attention to the uniformly high standards and variability of the erythema dosage in filtered radiation as determined by physicists and roentgenologists. For dermatologic purposes, except when malignant growths are being treated, it seems desirable to use the minimum or threshold erythema dose discussed by the authors, remembering that it may be doubled without marked intensification in the visible erythema but with considerable reduction in the limit of safety. If, for example, one uses 300 r, as advocated, for the erythema dose and gives a series of a dozen fractional doses in the treatment of a dermatosis, there is a far greater margin of safety in the cumulative effect than if one used 400 r as the erythema standard.

The authors have demonstrated a variability of 100 to 200 r in erythema dosage in the series of 30 cases in which tests were made by them. This should be empha-

sized, for one is too apt to accept a standardized average dose as the actual erythema dose for any given case. Goldsmith recently reported a difference in the number of roentgens required to produce erythema in 2 subjects, using the same factors in each case, greater than the difference noted for either subject when erythema tests were made with 55 and 95 kilovolts and either without filtration or with a 1 mm. aluminum filter. In Goldsmith's cases the tests produced a threshold erythema at an average of 300 r in one subject and of approximately 440 r in the other regardless of kilovoltage or filtration.

My co-workers and I have standardized our erythema dose at 350 r unfiltered, at 400 r for 1 mm. aluminum filter and at 450 r for 3 mm. aluminum filter, as compared with Dr. Cipollaro's figures of 300, 430 and 550 r, and we have obtained erythema uniformly at those figures. It appears that whatever standard is used for the erythema dose, one must not lose sight of the individual variability in the biologic reaction to roentgen rays, and I am in favor of making test doses on every one receiving serial treatments.

The authors have called attention to the uniformity of the epilation dose with different physical factors. In view of the apparent constancy of the former with moderate variations in filtration and voltage and in the rate of irradiation, would not the epilation dose be a better yardstick for measurement of doses than the erythema dose?

I have not worked with the supersoft roentgen ray, or grenz ray, but for some years after discontinuing the use of gas tubes, from which very soft radiation was obtainable, we carried out most of our vacuum tube irradiation at 30 kilovolts, believing that better results were thus obtained in dermatoses. Because of that clinical observation I believe there is a field for supersoft radiation, such as that obtained at 12 kilovolts, but it is important to heed the warning regarding the possibilities of telangiectasia and cutaneous atrophy following the use of the grenz ray.

Dr. C. Guy Lane, Boston: I was impressed, as I heard Dr. Cipollaro speak, with the changes which have taken place in the measurement of roentgen ray doses since the days when Dr. Pusey and Dr. Caldwell started out in this country with the measurement of doses for dermatologic conditions. Many changes have taken place, and they are still going on, and we are indebted to Dr. MacKee and Dr. Cipollaro for continuing the good work with reference to dosage with different types of filtration. There is need for further work in the comparison of the erythema and the epilation measurement of the dose with the use of modern measuring apparatus, such as the ionization chamber. They have pointed out the difficulties in estimating the erythema dose, the variations of the erythema, the consistency of the dose and its measurement by epilation. I am sure that the epilation dose, clinically speaking, is more accurate and perhaps can be widely used.

I was impressed, in a series of cases at our clinic some years ago, by the 100 per cent epilations we were having with 300 and the variation which occurred when we dropped our dose to 280 r. It did not seem possible that changing the dose to that extent might make a difference, but apparently it made a definite difference, in spite of the variation of some 20 per cent in the various subjects.

In accepting a standard dose, as was pointed out by Dr. Foerster in his discussion, one has also to think of the variation in dose used in different subjects. One should not necessarily accept such a standard for each person, for there are factors in the machine which may vary, as. Dr. Cipollaro has pointed out, and also factors in the individual, such as coloration, site of involvement and previous treatment, which should be taken into consideration.

I was interested also in the possible variation in the rate of administration. Some years ago a radiologist asked me whether there was any variation in the

cellular reaction if fractional treatment was given for a longer period, that is, if one-fourth skin unit was given in sixty seconds instead of ten seconds. I have a distinct impression, although I cannot prove it, that the use of a longer distance, 16 inches (40.6 cm.) for example, over a longer period of time has been better in some cases than using 8 inches (20.3 cm.) for a shorter time.

Dr. Anthony C. Cipollaro, New York: I have here a slide which shows the absorption curves with a diagrammatic drawing of the skin on ordinary graph paper. The curves represent the degree of absorption, in successive millimeters of skin, of radiations obtained with 10, 40, 60, 80 and 100 kilovolts without filtration and 137 kilovolts with a 3 mm. aluminum filter. Sixty-five per cent of the grenz rays (10 kilovolts) were absorbed by 0.5 mm. of skin. At this skin level only about 10 per cent of the 40 to 100 kilovolt beams were absorbed. At the 3 mm. level the grenz rays were almost entirely absorbed, whereas the 40 kilovolt roentgen ray beam was 45 per cent absorbed and the 100 kilovolt roentgen ray beam was 35 per cent absorbed. The difference in absorption at the 3 mm. level is so small that theoretically the same clinical results should be obtained with the 40 and 100 kilovolt radiations. These curves indicate in a rough way the quality of radiation that is best suited for a lesion situated at a particular level. They also indicate the limitations of the various qualities of radiation used in dermatologic therapy. There is only 15 per cent absorption at the 3 mm. level of the filtered roentgen ray beam (140 kilovolts and 3 mm. aluminum).

For unfiltered 100 kilovolt radiation, 300 r constitutes the erythema dose. This amount also causes epilation of the hair of the scalp in children. The definition of an erythema dose should contain a statement to cover epilation.

Dr. Andrews is right in saying that there is a difference in the number of roentgens required to produce erythema with different machines. Fewer roentgens will produce erythema with a valve rectified machine than with one mechanically rectified. This applies only to unfiltered radiation. With filtered radiation, there is no difference because the softer rays are absorbed by the filtering material.

I am glad that Dr. Lane called attention to the difference in epilation between 300 r and 280 r. That has been my experience. When the statement is made that radiation with 300 r is sufficient to produce erythema, the implication is that this quantity also causes epilation. With valve tube machines, erythema with an unfiltered 100 kilovolt roentgen ray beam may be obtained with as little as 226 r, and this quantity is not sufficient to cause epilation.

ELEPHANTIASIS OF THE LIPS AND OF THE MALE GENITALIA

WITH SPECIAL REFERENCE TO SYPHILIS AND LYMPHOGRANULOMA VENEREUM AS ETIOLOGIC FACTORS

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AND
GEORGE H. CURTIS, M.D.
CLEVELAND

Elephantiasis is a chronic disease of the cutaneous and subcutaneous tissues. It is characterized by inflammation and obstruction of the lymphatic vessels and subsequent hypertrophy and hyperplasia of the fibrous connective tissue. The lymph stasis and the resulting pachydermia produce persistent enlargement and gross deformity of the affected part of the body. The regions of predilection are the lower extremities and the external genitalia; the upper extremities, lips, ears and eyelids are less frequently affected. Elephantiasis may be congenital or acquired, but in this communication only certain acquired types will be considered.

Elephantiasis may be caused by many different factors. The etiologic importance of Filaria sanguinis hominis in endemic elephantiasis is well known. Removal of large amounts of lymph gland-bearing tissue in the surgical treatment of malignant tumor or of certain infections of the lymph nodes may be followed by chronic lymphedema and subsequent elephantiasis. Neoplastic processes of the lymph glands, Hodgkin's disease, chronic streptococcic lymphangitis, tuberculous and syphilitic adenitis and the lymphadenitis of lymphogranuloma venereum are common diseases producing lymph stasis that may terminate in elephantiasis.

In the era preceding the discovery of Spirochaeta pallida and the serologic reactions for syphilis and also before the advent of modern antisyphilitic remedies, syphilologists considered syphilis one of the principal causes of elephantiasis of the lips and of the external genitalia. Chronic ulcers of the vulva with elephantiasis, or "esthiomene of

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From the Cleveland Clinic.

Read at the Sixty-Second Annual Meeting of the American Dermatological Association, Inc., Monte-Bello, Quebec, Canada, June 2, 1939.

Hyguier,"[1] which is frequently accompanied by stricture of the rectum (the anorectal syphiloma of Fournier) was until a decade or so ago considered due to syphilis. Likewise, a chronic edematous condition of the lips described by Mracek and Lang[2] in 1888 and thirteen years later discussed in detail by Fournier[3] under the title of diffuse hypertrophic syphiloma has been referred to in the literature as syphilitic elephantiasis of the lips.

Since the recognition of lymphogranuloma venereum as a distinct entity and the discovery of a specific diagnostic test for this disease by Frei,[4] many reports have appeared which show conclusively that esthiomene and the anorectal syndrome described by Fournier are not due to syphilis but are manifestations of lymphogranuloma venereum. Also, recent reports indicate that the type of elephantiasis of the penis and scrotum that had heretofore been thought to be due to syphilis is in some cases analogous to esthiomene.

Some years ago, one of us (E. W. N.) observed 2 syphilitic patients with elephantiasis of the penis and scrotum. In neither case could the elephantiasis be explained on a basis of lymph stasis caused by any gross change in the superficial inguinal lymph glands. One patient had positive serologic reactions and neurologic signs which were consistent with the diagnosis of tabes dorsalis; the other patient had a positive Wassermann reaction of the blood and a history of an old syphilitic infection. A study of these patients was impossible, as they were observed only once. A few years later 2 other syphilitic patients were observed, each of whom presented, among other signs of the infection, an unusual persistent edematous enlargement of the lower lip. In both cases the clinical picture was identical with Fournier's description of diffuse hypertrophic syphiloma. More recently we have had the opportunity of studying a patient with elephantiasis of the penis and scrotum which was similar to that seen in the 2 cases aforementioned.

Elephantiasis of the type observed in these cases is rare. Fournier's description of syphilitic elephantiasis of the lip has apparently escaped the notice of authors of American textbooks on dermatology and syphilology for the past two or three decades, and the more recent works either contain brief comment only or fail to mention syphilis as a

1. Cole, H. N.: Lymphogranuloma Inguinale, Fourth-Venereal Disease: Its Relation to Stricture of the Rectum, J. A. M. A. **101**:1069-1076 (Sept. 30) 1933.

2. Mracek and Lang, cited by Petrov: Sur l'éléphantiasis syphilitique, Ann. d. mal. vén. **10**:337-355, 1915.

3. Fournier, J. A.: Traité de la syphilis: Tertiare période, Paris, J. Rueff, 1901, pp. 250-253.

4. Frei, W.: Eine neue Hautreaktion bei Lymphogranuloma inguinale, Klin. Wchnschr. **4**:2148-2149 (Nov. 5) 1925.

cause of elephantiasis. There are numerous reports pertaining to syphilitic elephantiasis, but with the recognition of lymphogranuloma venereum as a distinct entity and with better understanding of its various clinical manifestations the majority of these reports have become antiquated, and the importance previously attributed to syphilis as a cause of elephantiasis has greatly decreased. It now seems apparent that in some of the cases which have been reported as instances of syphilitic elephantiasis of the male genitalia the elephantiasic condition was in reality a manifestation of lymphogranuloma venereum. We have found few reports of cases in which syphilis could be considered the principal cause. Elephantiasis complicating extensive ulcerative gummatous infiltrations of the leg is most probably the result of secondary streptococcic lymphangitis.

In view of the present day concept that in some instances elephantiasis of the penis and scrotum is analogous to esthiomene, it would seem that inclusion of examples of Fournier's diffuse hypertrophic syphiloma in this discussion is unwarranted. This objection is only partially justified, because until recently both these conditions were considered by most observers to be syphilitic elephantiasis. Likewise, the pathogenesis of the type of elephantiasis of the lip under consideration is still undetermined, and there is reason to suspect that future observations may show lymphogranuloma venereum to be the chief etiologic factor in both these conditions.

The purposes of this report are: (1) to report 2 cases of the rare type of hypertrophy of the lips described by Fournier, (2) to report a case of elephantiasis of the male genitalia probably caused by lymphogranuloma venereum and (3) to discuss the similarity and probable relation between these two conditions.

SYPHILITIC ELEPHANTIASIS OF THE LIP

Review of the Literature.—In 1893, Eichhorst [5] reported a case of soft elephantiasis of the lips due to syphilis. The patient was a man who had had several mucocutaneous relapses, and during the fourth year of the infection redness of the nose and edema of the upper lip developed. The swelling spread to the lower lip, which became greatly deformed and reached the thickness of 2 thumbs. There were excessive salivation and bilateral rhagades. On palpation the lower lip was found to be soft and elastic. The swelling was painless. The submaxillary lymph nodes were enlarged but not tender. There was no fever and no history of recurrent erysipelas. While under observation the scrotum became enlarged, but this swelling disappeared later after the use of

5. Eichhorst, H.: Elephantiasis syphilitica der Lippen, Virchows Arch. f. path. Anat. **131**:568-573, 1893.

large doses of potassium iodide. The edema of the lips improved on administration of a mercury compound but recurred after the treatment was discontinued. Eichhorst stated that there were no true syphilomas of the lip in this case. He considered the swelling of the lip as soft elephantiasis due to syphilis and pointed out that syphilitic elephantiasis does not respond well to treatment.

Fournier [3] observed 15 cases in each of which chronic doughy edema of the lips produced such a striking change in the appearance of the patient that he thought the disease merited special consideration. His description of this deformity is excellent and detailed. He observed the condition only in the late stage of syphilis, usually between the tenth and the sixteenth year of the infection. In 12 cases only one lip was involved; in the remaining 3 both lips were enlarged. The swelling was limited to the lower lip in 10 cases. The massive enlargement of both lips produced a bizarre deformity of the mouth which was observed best in profile view, the lower lip appearing to be rolled outward. The lips retained their general form, and the color of the skin was unchanged. In some cases the mucous membrane of the lower lip showed indentations produced by pressure against the teeth. The enlarged lips were soft, could not be pitted and on palpation felt clammy and elastic. The enlargement was accompanied by drooling and by difficulty in articulation and mastication. The regional lymph glands were not enlarged, and there was no pain, either spontaneous or provoked. The onset of the edema was insidious, but after the condition was fully established the size of the lips remained constant for years. In 1 of Fournier's patients the hypertrophy had transformed the lower lip into a sausage-like mass that had remained unchanged for eight years. Late cutaneous syphilids involving the nose and chin were coexisting lesions in some cases, and frequently there was an accompanying sclerous form of late syphilitic glossitis which the author thought was in some way related to the enlargement of the lip. He referred to a case that Mracek had observed in which the lesion invaded the nose and tongue. Fournier was unable to obtain a complete cure of the condition, but in some cases the hypertrophy was noticeably decreased on intensive treatment with potassium iodide, injections of mild mercurous chloride and continuous compression by an india rubber dressing.

Whitfield [6] reported a case of chronic enlargement of the lips due to syphilitic lymphangitis similar to that observed by Fournier. The patient was a man who had a syphilitic infection of fourteen years' duration. During the eighth year extensive late syphilids developed on the legs, and three years later the lips and the prepuce became swollen.

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6. Whitfield, A.: Chronic Enlargement of the Lips Due to Syphilitic Lymphangitis, Proc. Roy. Soc. Med. (Dermat. Sect.) **2**:99-102, 1908-1909.

A large part of the prepuce had been excised, but there still remained a certain amount of elephantiasis of the penis. When the patient was first seen by Whitfield there were an enormous enlargement of the lips (particularly of the lower lip), ulcers of the commissures of the lips, impetiginous syphilids in the scalp and chronic superficial syphilitic glossitis. The glossitis and cutaneous lesions responded favorably to antisyphilitic treatment. The lips became more pliable and comfortable, but the deformity did not disappear. Whitfield felt that the labial enlargement was caused by syphilitic lymphangitis. In the discussion of this case Macleod referred to 2 similar cases which he had observed and stated that it is difficult to treat such conditions successfully. The coexisting elephantiasis of the lips and of the penis in this case was probably not accidental. The significance of this observation will be discussed later.

Montgomery and Culver [7] reported a case of hypertrophy of the lower lip associated with late nodular syphilids on the chin and at the commissures of the lips. The syphilomas disappeared rapidly after the administration of arsphenamine, but the residual elephantiasis disappeared slowly. This case differs from ours and from those reported by Fournier and by Whitfield in that the enlargement of the lip was due to gummatous infiltrations; however, the elephantiasis which remained after the rapid disappearance of the nodular syphilis probably was similar to that observed in other cases.

Under the title "Syphilome en nappe" Tuffier [8] described and differentiated in detail a tertiary lesion of the lip characterized by uniform hypertrophy with moderate induration, superficial ulcerations of the mucosa and red-violet pigmentation of the skin. In some weeks the lip became everted and enlarged to two or three times its normal size. Untreated, the lip after months showed scarring and atrophy, with an irregular lobulated contour. In the early stages of the condition the lesion could be made to disappear by antisyphilitic treatment, but after it became sclerosed it did not respond.

Some observers have confused this lesion with the diffuse hypertrophic syphiloma of Fournier, although there is only a superficial resemblance.

New and Kirch [9] reported 67 cases of chronic noninflammatory permanent enlargement of the lips and face which they concluded was a

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7. Montgomery, D. W., and Culver, G. D.: Enlargement of the Lower Lip from Syphilis, Am. J. Syph. **6**:55-57 (Jan.) 1922.

8. Tuffier: Gommes et scléroses syphilitiques des lévres: Labialites tertiaires, Rev. de chir. **6**:777-812, 1886.

9. New, G. B., and Kirch, W. A.: Permanent Enlargement of the Lips and Face Secondary to Recurring Swellings and Associated with Facial Paralysis: A Clinical Entity, J. A. M. A. **100**:1230-1233 (April 22) 1933.

clinical entity. The lips and cheeks were most frequently involved by a diffuse, soft nonpitting swelling. Peripheral paralysis of the facial nerve occurred in 13 cases. Histologic examination showed only edematous tissue containing lymphocytes. The cause of the edema was not determined; however, the authors stated that general examination revealed nothing that might bear any relation to the condition. They did not state the incidence of syphilis in their cases, and there is no reason to think that they considered lymphogranuloma venereum a possible etiologic factor. The edema in these cases was similar to that associated with diffuse hypertrophic syphiloma; but apparently concomitant manifestations of late syphilis were absent in all cases. Paralysis of the facial nerve is not a part of Fournier's syndrome.

Reference should be made to a case presented by Weidman and Hunter [10] before the Philadelphia Dermatological Society. The patient was a Negro aged 35 years who had had edema of the eyelids for five years as well as edema of the penis and scrotum and a generalized patchy pigmentary eruption. The Frei reaction was positive, and the albumin-globulin ratio was reversed. Weidman raised the question whether the edema was one more cutaneous manifestation of lymphogranuloma venereum.

Fournier's diffuse hypertrophic syphiloma is a rare condition. We were unable to find a case of this condition reported in the American literature. The following 2 cases have been observed at the Cleveland Clinic.

REPORT OF CASES

CASE 1.—A white man aged 42 was admitted to the clinic on Oct. 4, 1926. His chief complaint was swelling of the lips. The family and marital histories were unimportant. In 1903, a penile lesion developed after coitus. It was cauterized and treated with topical remedies. The patient had never received antisyphilitic treatment.

In 1925, after some dental work, one side of the lower lip began to swell. The swelling gradually spread to involve the whole lip. A few days before we first saw him the upper lip began to enlarge and a fissure appeared at the left corner of the mouth. The swelling of the lips had been painless. At no time had he had erysipelas or recurrent attacks of acute cellulitis of the face or lips. Applications of heat and one roentgen ray treatment (dose unknown) had failed to alter the swelling.

The patient was well developed and well nourished. With the exception of hypertrophy of the lower lip, physical examination gave normal results. The lower lip was diffusely enlarged to approximately twice its normal size, with little change in its general outline. It was soft and elastic; it could not be pitted, and its cutaneous surface was normal in color. In profile the lower lip appeared to be rolled outward. The vermilion margin was smooth but considerably

10. Weidman, F. D., and Hunter, R.: Lymphogranulomatosis Inguinalis: Edema of the Eyelids of Undetermined Nature, Arch. Dermat. & Syph. **34**:342 (Aug.) 1936.

enlarged. Because of an excessive flow of saliva there was a superficial, perlèche-like erosion at the left commissure of the lips. The upper lip was slightly enlarged. The submaxillary lymph glands were not enlarged, and there were no signs of gummatous infiltration of the skin of the lips or of the face. The Wassermann and Kahn reactions of the blood were strongly positive (4 plus). Other laboratory tests revealed no abnormality. Biopsy was not performed.

A diagnosis of syphilitic elephantiasis of the lower lip was made, and antisyphilitic therapy was started. From Oct. 11, 1926 to March 26, 1927 the patient received four injections of potassium bismuth tartrate (0.4 Gm.), four injections of mercury salicylate (0.26 Gm.) and seven injections of neoarsphenamine (5.4 Gm.). Increasing doses of saturated solution of potassium iodide were taken by mouth. As this amount of antisyphilitic medication produced only a slight decrease in the size of the lip, the patient became discouraged and discontinued treatment. He has not been observed since.

Case 2.—A white man aged 32 came to the clinic on Nov. 22, 1933, complaining of an eruption on the left arm and left hand and an enlargement of the lower lip. His family history and marital history were not important. Gonorrhea and syphilis had been contracted in 1920. The only antisyphilitic treatment which he had received consisted of four intramuscular injections in 1920.

About one year before he was first seen the lower lip was bruised in a fist fight, but the mucocutaneous surfaces were not broken. The lip was painful and swollen for a week. One month later the lower lip began to increase in size, and up to six months before we saw him there were periods of remission and exacerbation. Since then there had been a gradual enlargement. There were no subjective symptoms, and the hypertrophy of the lip was not preceded by erysipelas.

A month previously he had injured the left hand, and an eruption developed at the site of the injury. He had recently been treated by his family physician for "ringworm" infection on the left arm.

The hypertrophy of the lip and the cutaneous lesions were the only significant abnormalities found on physical examination. On the dorsal surface of the left hand and the extensor surface of the left arm were late nodular ulcerative syphilids. There was a dull red, granulomatous nodule involving the skin in the middle of the upper lip. A painless, soft, elastic, diffuse enlargement of the lower lip gave the patient a bizarre appearance (fig. 1). No nodules or other clinical evidences of a granulomatous infiltration were found in the lower lip. The lip maintained its normal form and could not be pitted or decreased in size by compression. The labial eversion emphasized by Fournier was well demonstrated and was seen best in the profile view. There was a smooth, irregular atrophic scar on the enlarged vermilion surface of the right side of the lower lip. The submaxillary glands were not enlarged. The Wassermann and Kahn reactions were strongly positive. The patient refused to submit to a lumbar puncture or to permit a biopsy.

A clinical diagnosis of late cutaneous syphilis and syphilitic elephantiasis was made, and antisyphilitic treatment was begun. The patient discontinued treatment after he had received six intramuscular injections of bismuth salicylate. Potassium iodide was taken by mouth. The syphilids responded favorably to treatment, but at our last observation we were unable to detect any improvement in the hypertrophy of the lower lip. The patient was advised to have the deformity of the lip surgically corrected, but he would not consent. Although this patient presented unmistakable manifestations of late cutaneous syphilis, it is regrettable that a test with Frei antigen was not made.

In our opinion the hypertrophy of the lip in these 2 cases was identical with Fournier's diffuse hypertrophic syphiloma. The process began in the lip and progressed rapidly until the lip was twice its normal size. The hypertrophy did not destroy the normal form of the lip and remained unchanged in spite of antisyphilitic treatment. The enlarged lip was not indurated; instead, it was soft, elastic and doughy and did not pit on pressure. The regional lymph glands were not enlarged. We were unable to find a lesion in the mouth or in the neck which would explain the elephantiasis. We believe that absence of acute febrile reactions or attacks of erysipelas preceding the hypertrophy was sufficient reason for excluding the possibility of elephantiasis nostras. The

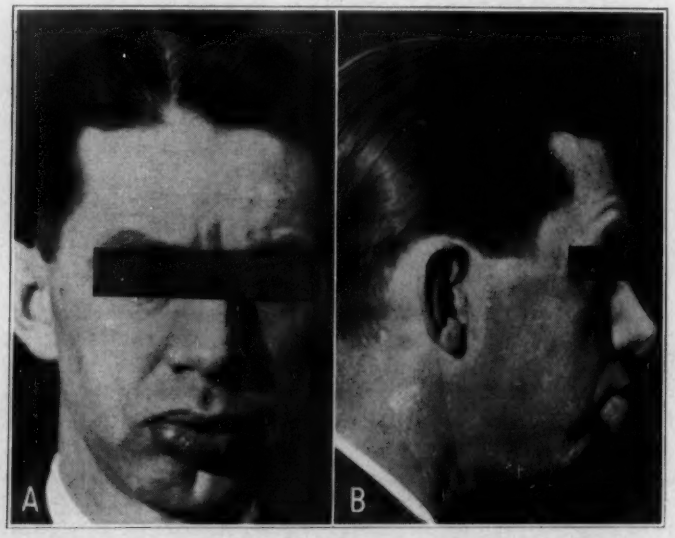

Fig. 1 (case 2).—*A*, Hypertrophy of the lower lip with a small gummatous nodule on upper lip. *B*, eversion of the lower lip.

doughy, elastic feel of the lip, the rapid appearance of the hypertrophy and the fact that the lip retained its normal form made the diagnosis of lymphangioma untenable.

In our 2 cases the point of interest is the questionable importance of syphilis in the causation of elephantiasis. The inefficacy of modern antisyphilitic remedies in this condition not only suggests that the pathologic changes in the lip were not gummatous but arouses suspicion as to the importance of syphilis as an etiologic factor.

SYPHILITIC ELEPHANTIASIS OF THE MALE GENITALIA

Until a few years ago the same uncertainty existed regarding the importance of syphilis as a cause of elephantiasis of the genitalia.

Numerous cases of syphilitic elephantiasis of the penis and scrotum have been reported, but in only a few which we have reviewed was there sufficient evidence to warrant such a diagnosis.

Edema of the male genitalia terminating in elephantiasis may be initiated by a syphilitic infection in one of the following ways:

1. By extensive syphilitic adenitis of the inguinal and pelvic lymph nodes.

2. By diffuse syphilitic inflammation of the prepuce and scrotum.

3. By pure syphilitic lymphangitis of the genitalia.

4. By ulcerative syphilids of the leg or of the genitocrural region complicated by secondary streptococcic lymphangitis.

The first two conditions are rare, and it is doubtful whether a syphilitic inflammatory reaction limited mainly to the lymphatics ever occurs. In many of the reported cases of so-called syphilitic elephantiasis of the penis and scrotum which we have reviewed complicating streptococcic lymphangitis was the most probable cause. We have eliminated all cases reported as instances of syphilitic elephantiasis of the male genitalia in which it seemed that secondary streptococcic lymphangitis was the major etiologic factor. However, rare cases of elephantiasis of the penis and scrotum have been reported in which it was reasonably certain that syphilis was the true cause.

Review of the Literature.—In a comprehensive discussion of elephantiasis, Petrov [11] stated that syphilis does not play as important a role in the causation of elephantiasis as has been maintained by many observers. He pointed out that syphilitic elephantiasis ordinarily develops in the tertiary stage of the disease and that the genitalia were affected in 32 per cent of cases studied by him, while the lip was involved in only 1.5 per cent. Petrov reported a case of syphilitic elephantiasis of the penis and scrotum. The genitalia were three times their normal size. The skin of the scrotum was bluish and indurated and did not pit on pressure. There was no pain. There were numerous verrucous elevations separated by sulci from which could be expressed a seropurulent exudate. On the clinical findings the diagnosis rested between syphilis and tuberculosis. Cultures of material obtained from the sulci showed only staphylococci. The von Pirquet reaction was negative, but the Wassermann reaction was positive. The histologic changes consisted of hypertrophy of the connective tissue, dilatation of the blood and lymphatic vessels and perivascular infiltration with small lymphocytes, mast cells and plasma cells. There were pronounced endarteritis and endophlebitis. After two months of antisyphilitic

11. Petrov: Sur l'éléphantiasis syphilitique, Ann. d. mal. vén. **10**:337-355, 1915.

treatment with potassium iodide and mercury compounds the penis was of normal size, but the scrotum had decreased to half its original size. The verrucous elevations were unchanged. The induration of the skin of the scrotum had not completely disappeared. The author stated that in syphilitic elephantiasis antisyphilitic therapy does not diminish the affected organs beyond a certain point.

McDonagh [12] observed a man aged 46 in whom eighteen years after syphilis was contracted, nonulcerative late syphilis developed on the buttock and on the left half of the scrotum. One year later the scrotum began to enlarge. Eleven years afterward, when this patient came under observation, the syphilids of the scrotum had disappeared, but there was superficial glossitis. The penis was buried in an enlarged scrotum which measured 28½ inches (72.4 cm.) in circumference. The Wassermann reaction was positive. After thirteen injections of gray oil (a mixture of olive oil and hydrous wool fat, containing mercury) the scrotum measured 13½ inches (34.2 cm.) in circumference, the skin was softer and the testicles and penis were normal. Histologic changes in the scrotum consisted chiefly of a decided increase in connective tissue elements, dilated lymph spaces surrounded by a layer of endothelial cells and infiltrations of lymphocytes and plasma cells. The arteries and veins were practically unchanged. McDonagh stated the opinion that this case was an example of syphilitic lymphangitis. In his discussion Pringle stated that he had been unable to find definite evidence of syphilitic lymphangitis recorded in the literature.

Emery and Glantenay [13] reported the case of a man aged 45 with a syphilitic infection of twenty years' duration in whom severe edema of the prepuce developed suddenly and without apparent cause. After a series of partial remissions the prepuce gradually became thickened and sclerosed. At the end of two years the penis was two or three times its normal size, and the scrotum began to enlarge. Ten years prior to the onset of the edema, la[illegible]ular syphilids appeared on the thighs and buttocks and later on other parts of the body. The enlargement of the genitalia was without pain or evidence of an acute inflammatory reaction in the skin of the penis or that of the scrotum. The authors pointed out that the onset and clinical characteristics of the elephantiasic condition in this case were identical with those seen in cases of diffuse hypertrophic syphiloma of the lip. In a discussion of this case Fournier stated that he was convinced that the lesions were syphilitic and that

12. McDonagh, J. E. R.: Syphilitic Elephantiasis of the Scrotum (Lymphangitis), Brit. J. Dermat. **24**:24-27, 1912.

13. Emery and Glantenay: Éléphantiasis des organes génitaux externes, Bull. Soc. franç. de dermat. et syph. **9**:150-151, 1898.

the syphiloma of the lip offered comparable characteristics. Although the effect of antisyphilitic treatment was not recorded, it should be pointed out that the mode of onset, the coexisting late syphilids and the character of the elephantiasis were similar to those of diffuse hypertrophic syphiloma of the lips.

Levy-Bing and Gerbay [14] reported 2 cases of elephantiasis of the male genitalia which they considered to be uncontestably of syphilitic origin. The first case was that of a man aged 26 in whom elephantiasis or edema of the scrotum developed during the secondary stage of syphilis. There were two chancres on the scrotum and one on each side of the median raphe. The scrotum was twice its normal size, and there was marked edema of the skin in the pubic region. There was a decided bilateral enlargement of the lymph glands. The extensive regional syphilitic lymphadenitis was the cause of the lymphedema of the scrotum. The authors stated that this case was an example of an uncommon yet well known type of syphilitic elephantiasis of the genitalia. In this type the elephantiasis is always secondary to a preexisting syphilitic lesion.

Their second patient was a man aged 22 in whom severe edema of the penis and scrotum developed without any preceding or concomitant lesion of the skin or mucous membrane. In each inguinal region there were four or five firm, movable lymph glands the size of small almonds. The Wassermann reaction was strongly positive. With antisyphilitic treatment there was a prompt return of the genital organs to their normal size.

These cases were reported as examples of syphilitic elephantiasis. It seems to us that changes characteristic of elephantiasis were not present and that syphilitic lymphedema would be a more accurate term.

The only acceptable case of syphilitic elephantiasis of the male genitalia which we found in the American literature was a case reported by Marshall.[15] The patient was a Negro aged 30 in whom an enlargement of the genitalia developed thirteen years after he had contracted syphilis. There were no concomitant late syphilids. A careful search for streptococci in the skin of the scrotum was made, but none were observed. The superficial lymph glands were enlarged. The Wassermann reaction of the blood was strongly positive. The skin of the genitalia was firm and thickened and did not pit on pressure. The histologic changes consisted mainly of increase in the fibrous connective

14. Levy-Bing and Gerbay: Deux cas d'éléphantiasis syphilitique des organes génitaux, Ann. d. mal. vén. **13**:600-609, 1918.

15. Marshall, C. H.: Syphilitic Elephantiasis of the Scrotum, J. A. M. A. **85**: 875-877 (Sept. 19) 1925.

tissue and perivascular infiltration with small lymphocytes, plasma cells and a few mast cells. There were numerous dilated lymph spaces, and many of the smaller arterioles were obliterated. Prompt and decided improvement followed antisyphilitic treatment.

Apparently there is little doubt that in rare cases elephantiasis of the male genitalia is of syphilitic origin. However, for years various observers have reported cases of sporadic elephantiasis of the penis and scrotum in which no definite etiologic agent could be found. In some cases there were unmistakable concomitant signs of syphilis but antisyphilitic treatment failed to influence the elephantiasis. In others there was no adequate explanation for the enlargement of the genitalia. It is probable that the elephantiasis which was erroneously considered to be of syphilitic origin in some of these cases was actually caused by the virus of lymphogranuloma venereum.

ELEPHANTIASIS OF THE MALE GENITALIA DUE TO LYMPHOGRANULOMA VENEREUM

Review of the Literature.—Barthels and Biberstein [16] were the first to point out that in rare cases an existing lymphogranulomatosis inguinalis may cause an elephantiasis of the male genitalia which is a counterpart to esthiomene. Their patient was a man aged 31 who at the age of 21 had what was thought to be a soft chancre. At that time the glands were removed from the inguinal regions on both sides. From time to time the patient had swellings of the penis and scrotum, which always subsided without treatment. Nine weeks before he came to the clinic a swelling of the penis and scrotum suddenly developed and persisted. The Frei reaction was strongly positive. Serologic reactions and tests for a previous infection with Ducrey's bacillus were negative. A portion of the edematous skin was removed, and two weeks later there were lymph fistulas. Six months later abscesses appeared in the scrotum and groin. The histologic changes in the elephantiasic tissue were similar to those which are observed in the lymph glands in cases of lymphogranuloma venereum and in tissues in the presence of the anorectal syndrome. The authors felt that blockage of the flow of lymph by changes in the glands was not sufficient to cause the elephantiasis but that specific inflammatory changes seen in the peripheral lymph vessels added to the obstruction of lymph flow in the genitalia. They believed that recanalization of thrombosed lymph vessels accounted for the early spontaneous disappearance of the edema in their case.

16. Barthels, C., and Biberstein, H.: Elephantiasis penis et scroti und Lymphogranulomatosis inguinalis, Beitr. z. klin. Chir. **152**:325-338, 1931.

They suggested that the virus of lymphogranuloma venereum varies in virulence from time to time and that it may remain in the tissues in a latent state.

Stryker and Ploch [17] were the first in the United States to report a case of elephantiasis of the penis and scrotum in which lymphogranuloma venereum was the etiologic agent.

Navarro Martin [18] reported a case of lymphogranulomatous elephantiasis of the penis and scrotum with concomitant stricture of the rectum. Cole [1] observed a similar case. Equally significant are the observations of de Gregorio,[19] who reported a case of elephantiasis of the penis due to a chronic lymphogranulomatous ulcer in the balanopreputial region. This patient's wife became infected and later had rectal stenosis.

Coutts and Ahumada [20] reviewed the literature pertaining to the cutaneous manifestations of lymphogranuloma venereum and reported a case, describing an unusual lymphogranulomatous syndrome. A man aged 36 who had previously contracted syphilis and gonorrhea later had a slight urethral discharge which subsided without treatment. At about the same time the genitalia began to enlarge. Within six months the penis and scrotum were considerably increased in size and squamous lesions began to appear on the legs and gluteal regions. The cutaneous lesions eventually became large psoriasiform plaques, and in certain areas ulcerations appeared which simulated ecthyma.

The Wassermann reaction, the lymphatic reaction and the Kahn reaction were positive. The intradermal Frei test gave a negative reaction, but an antigen prepared from the cutaneous lesions gave a positive reaction in patients with lymphogranulomatous syndromes and a negative reaction in healthy controls. No statement was made regarding the effect of antisyphilitic treatment on the cutaneous lesions or the elephantiasis of the genitalia.

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17. Stryker, G. V., and Ploch, B.: Elephantiasis of Penis and Scrotum: A Sequela of Lymphogranuloma Inguinale, Arch. Dermat. & Syph. **32**:86-89 (July) 1935.

18. Navarro Martin, A.: Elefantiasis peneoescrotal de origen linfogranulomatoso, Actas dermo-sif. **27**:425-430 (Jan.) 1935.

19. de Gregorio, E.: Ulcération chronique et éléphantiasis de la verge et sténose rectale conjugale dans la maladie de Nicolas-Favre, Rev. franç. de dermat. et de vénéreol. **12**:259-271 (May) 1936.

20. Coutts, W. E., and Ahumada, H.: Penoscrotal Elephantiasis of Lymphogranulomatous Origin: Description of a Case with Psoriasiform Cutaneous Lesions and Others Resembling Ecthymatous Pyoderma, Arch. Dermat. & Syph. **36**:1014-1017 (Nov.) 1937.

In a review of this case, Wise and Sulzberger [21] raised the question of positive anergy as an explanation for the negative Frei reaction of this patient.

A few more cases of elephantiasis of the male genitalia caused by lymphogranuloma venereum have been reported (Coutts and Herrera; [22] Nicolas, Lebeuf and Charpy; [23] Vigne, Bonnet and Lombard.[24]

It is well known that in lymphogranuloma venereum there is a great discrepancy in the incidence of suppuration of the inguinal lymph nodes, the anorectal syndrome and elephantiasis of the genitalia in men and women. The reason for this variance is the difference in the lymphatic circulation of the genitalia, the anus and the rectum in the male and in the female. This fact has been adequately discussed by Barthels and Biberstein,[25] Cole,[1] Bloom [26] and others; therefore we have omitted a description of these anatomic differences.

REPORT OF A CASE

A white man aged 60 came to the clinic on Nov. 17, 1937, complaining of an enlargement of the penis and scrotum. The family history and marital history were unimportant. The patient had had typhoid fever at the age of 30 and eight years later had contracted malaria while serving with the army in the Philippine Islands. At this time he suffered an attack of jaundice. He continued to have about one attack of "chills and fever" every year. For years he drank alcoholic beverages to excess, but in recent months he had been more temperate. He denied having had gonorrhea but stated that at the age of 25 he had a sore on the penis. This lesion was cauterized and disappeared within two weeks. He was certain that a generalized eruption did not develop, but he did have a suppuration of the inguinal lymph nodes on the right with subsequent sinus formation lasting several weeks. He had never received antisyphilitic treatment, and recent Wassermann reactions were reported to have been negative.

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21. Wise, F., and Sulzberger, M. B.: Year Book of Dermatology and Syphilology, Chicago, The Year Book Publishers, Inc., 1938, p. 372.

22. Coutts, W. E., and Martini Herrera, J.: Elephantiasis penis et scroti in ihrer Beziehung zur Lymphogranulomatosis venerea, Dermat. Wchnschr. **98**:784-785 (June 23) 1934.

23. Nicolas, J.; Lebeuf, F., and Charpy, J.: Eléphantiasis génital chez un malade opéré, il y a 18 mois, pour maladie de Nicolas-Favre: Etude des intradermoréactions, Bull. Soc. franç. de dermat. et syph. **39**:27-28 (Jan.) 1932.

24. Vigne, P.; Bonnet, J., and Lombard, R.: Eléphantiasis de la verge consécutif à un évidement ganglionnaire bilatéral ancien pour maladie de Nicolas-Favre, Marseille-méd. **1**:463-465 (April 25) 1937.

25. Barthels, C., and Biberstein, H.: Zur Aetiologie der "entzündlichen" Rektumstrikturen (Lymphogranulomatosis inguinalis als Grundkrankheit), Beitr. z. klin. Chir. **152**:161-183, 1931.

26. Bloom, D.: Strictures of the Rectum Due to Lymphogranuloma Inguinale, Surg., Gynec. & Obst. **58**:827-840 (May) 1934.

The present illness began about 1928. The initial manifestation consisted of moderate thickening of the scrotum accompanied by mild pruritus. These changes were of minor importance until two years later, when suddenly the penis and scrotum greatly increased in size. There were no concomitant lesions of the genitocrural region that could have been considered as a cause for the enlargement of the genitalia. On the day before the sudden changes occurred the patient lifted a very heavy object; consequently, he attributed his difficulty to the strain. During the past seven years there had been no decrease in the size of the genitalia.

Fig. 2 (case 3).—Elephantiasis of the penis and scrotum.

The subjective symptoms disappeared with the onset of elephantiasis. Coitus was impossible, and the patient had been impotent for the past seven years (fig. 2).

With the exception of enlargement of the genitalia, physical examination showed only a few minor abnormalities. There was a slight impairment of hearing, and the sclerae were yellowish. Many teeth were carious, and there was chronic gingivitis. The liver was not palpable. Roentgen examination of the chest, gastrointestinal tract and genitourinary system revealed no abnormality. The prostate was moderately enlarged.

The most striking abnormality was enlargement of the genitalia. The scrotum was about the size of a small grapefruit, and the penis was correspondingly

Fig. 3 (case 3).—Section from the scrotum, showing edema, dilatation of vessels and hypertrophy and hyperplasia of connective tissue; × 150.

enlarged. The scrotum, the prepuce and the skin of the penis were edematous. Firm digital pressure produced slight pitting. The normal cutaneous markings were accentuated, but there were no lymph vesicles or verrucous papules on the scrotum or on the penis. The color of the scrotum varied only slightly from normal, except in the more dependent portion, which was dull pinkish blue. There were no discharging sinuses and no urethral discharge. The glans penis could not be exposed. The testicles were apparently of normal size. There was a scar in the right inguinal region.

The routine blood cell and differential counts were normal. The sedimentation rate was 0.76 mm. per minute. The icterus index was 20 units. A red blood cell fragility test showed beginning hemolysis at 0.55 per cent and complete hemolysis at 0.38 per cent. The value for serum protein was 5.3 Gm. per hundred cubic centimeters (albumin 4.1 Gm.; globulin, 1.2 Gm.). The Wassermann and Kahn reactions were negative. The spinal fluid was normal. Repeated examinations for filaria and plasmodia gave negative results. Bromsulphalein and Takata-Ara tests indicated a slight impairment of hepatic function. The Frei reaction was strongly positive.

Dr. E. Perry McCullagh of the department of endocrinology made studies to determine whether the prolonged insulation of the testicles by the greatly thickened scrotum had altered the gonadal function. An assay for estrogen showed 20 to 30 rat units per daily output of urine (normal, 30 to 60 units). The Friedman test showed slight traces of gonadotropic hormone, and a quantitative assay for androgenic substance showed 16.9 international units (normal, 20 to 80 units).

Histologic Examination.—Tissue for histologic examination was removed from the right side of the scrotum.

Epidermis: Changes in the corium had obliterated most of the papillae and had reduced the epidermis to five or six layers of cells. The surface of the epidermis was covered by a thin hyperkeratotic layer. There was no parakeratosis. The granular layer consisted of one layer of cells. The rete mucosum showed moderate intercellular edema, and the basal layer was intact (fig. 3).

Corium: There was an enormous increase in thickness of the corium. There were diffuse edema and great hypertrophy and hyperplasia of the connective tissue. These changes extended into the subcutaneous tissue. The edema was most marked in the upper part of the corium. The blood and lymph vessels in the papillary and subpapillary layers were greatly dilated. Perivascular edema was most prominent about the larger vessels. There were few areas of cellular infiltration; however, fibroblasts and numerous connective tissue nuclei were scattered throughout the corium. The fibers of the dartos were edematous and stained poorly, and in many places the cytoplasm had disappeared, leaving deeply stained nuclei surrounded by clear spaces. This degeneration and final vacuolization were more marked in some muscle bundles than in others (fig. 4).

In the lower portion of the section and in the dense trabeculae of the dartos there were a few small, well circumscribed areas of closely packed small lymphocytes. There were no giant cells or areas of cellular infiltration of a granulomatous type. The sweat and sebaceous glands were sparse but normal.

Diagnosis.—A diagnosis of cirrhosis of the liver and congenital hemolytic jaundice was made by Dr. Russell L. Haden. The enlargement of the genitalia was considered to be a manifestation of lymphogranuloma venereum.

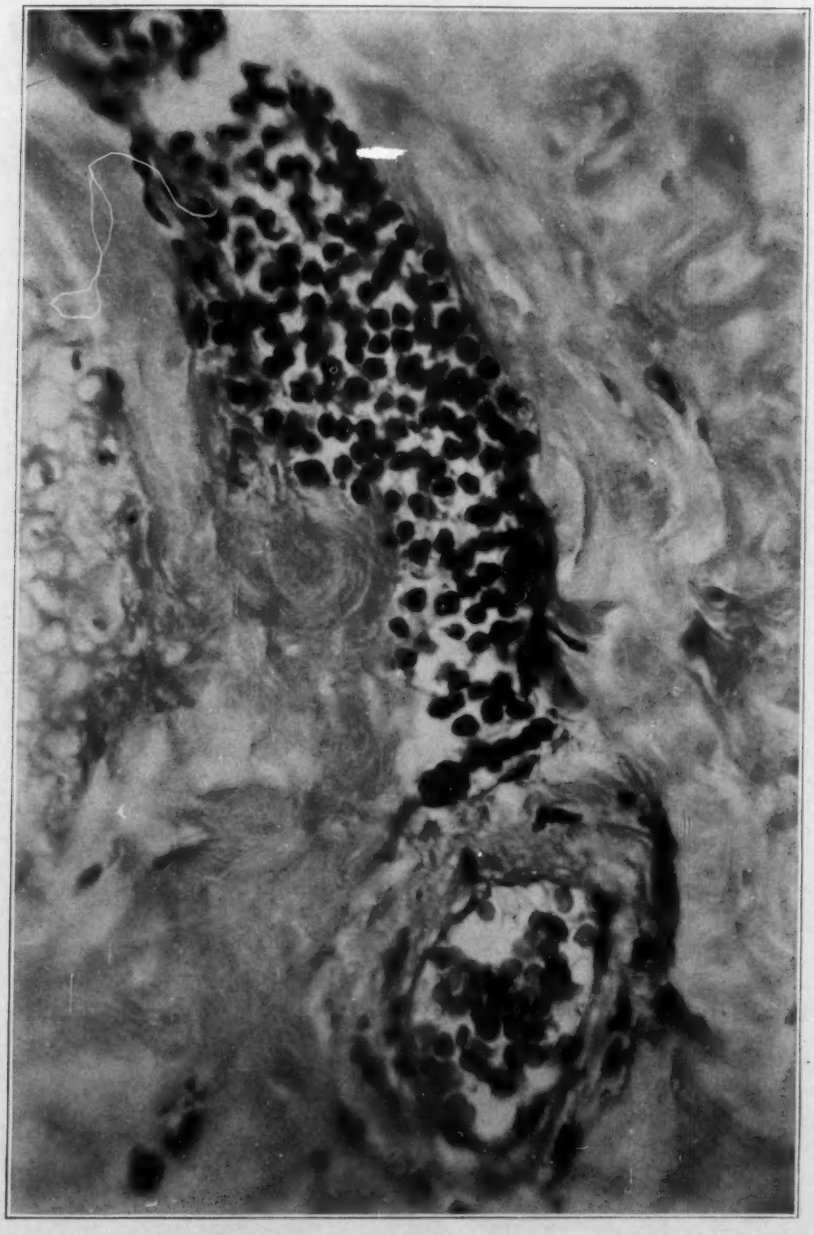

Fig. 4 (case 3).—Dilatation of an arteriole, perivascular edema and an area of lymphocytic infiltration in the deeper portion of the corium; × 600.

COMMENT

The cases presented here are examples of a rare and unusual elephantiasis. Elephantiasis of the scrotum from any cause is an unusual condition, and judging from the scarcity of reports during the past three decades the elephantiasic enlargement of the lip which was observed in our cases is almost a forgotten entity. The rolled-out, doughty, elastic, diffuse, symptomless enlargement of the lips occurring without preceding acute cellulitis and without enlargement of the regional lymph glands or distortion of the normal form of the lip constitutes a condition of which there is no counterpart.

Although this condition has been reported as occurring only in syphilitic persons, there is reason to doubt that syphilis is the true cause. The rarity of the disease precludes an extensive investigation of this problem by a single observer. All observers have based their opinions regarding the nature of Fournier's diffuse hypertrophic syphiloma on clinical findings. So far as we have been able to determine, no one has studied the pathologic character of this condition, and until some one is able to obtain tissue for histologic examination the nature of the hypertrophy will remain obscure. We deeply regret our inability to obtain the permission of our second patient for a biopsy and also realize that our failure to do a Frei test somewhat decreases the value of this report. However, a positive Frei reaction would only have indicated the coexistence of syphilis and lymphogranuloma venereum and could not have been considered conclusive proof that the enlargement of the lip was of lymphogranulomatous origin. A study of the histologic changes in the lip would have been of greater importance.

Is the elephantiasis of the lip in these cases of syphilitic origin? If not, is there any reason to suspect that, as in some cases of elephantiasis of the genitalia, lymphogranuloma venereum may be the cause? The only approach to this problem is to attempt to correlate certain significant features of the cases that have been reported with the present concept of lymphogranuloma venereum and elephantiasis.

In all of the cases which we have reviewed, the enlarged lip was soft, elastic and free of palpable infiltration. These characteristics are not compatible with the presence of gummatous infiltration. Also, it is significant that while the enlargement of the lip remained unchanged, the concomitant mucocutaneous manifestations of late syphilis responded favorably and promptly to antisyphilitic treatment. We are cognizant that in rare cases a gummatous lesion fails to respond favorably to antisyphilitic therapy; however, in such cases any coexisting late syphilid is likewise resistant to treatment. In view of these facts we feel that there is reason to doubt seriously the syphilitic origin of Fournier's diffuse hypertrophic syphiloma.

Although we are without substantial evidence, we feel that there is sufficient reason for suspecting that this type of elephantiasis of the lip may be caused by lymphogranuloma venereum. Syphilis and lymphogranuloma venereum are usually of venereal origin and are frequently coexisting infections. Some patients with esthiomene and the anorectal syndrome have had both diseases, and, although concomitant manifestations of syphilis disappeared under antisyphilitic treatment, the elephantiasis of the vulva and rectal stenosis remained unchanged. Identical observations have been reported in cases of elephantiasis of the penis and scrotum of probable lymphogranulomatous origin. Of particular interest is the case reported by Whitfield, in which enlargement of the lips was preceded by elephantiasis of the genitalia of unexplained origin. The concomitant syphilids disappeared under antisyphilitic treatment, but the elephantiasis was altered only slightly. The case reported by Weidman and Hunter, in which chronic edema of the eyelids, penis and scrotum occurred in a patient with lymphogranuloma venereum, should be cited as additional presumptive clinical evidence of the lymphogranulomatous origin of certain elephantiasic conditions of the lips, face and eyelids.

The clinical characteristics of diffuse hypertrophic syphiloma and of lymphogranulomatous elephantiasis of the penis and scrotum are similar. In both conditions there is usually a history of a venereal infection several years prior to the onset of elephantiasis. The enlargement begins insidiously without any apparent cause and frequently progresses suddenly to a certain point, remaining unchanged for several years. The elastic, symptomless, nonpitting edema is similar in the two conditions.

Barthels and Biberstein's observations indicate that the virus of lymphogranuloma venereum may remain dormant in the tissues and when activated may produce lymphangitis and lymph stasis which may terminate in elephantiasis. Since lymphogranuloma venereum is a systemic infection, it is not unreasonable to believe that such changes may be incited by this virus in portions of the body remote from the genitalia and the rectum.

We believe that there are good reasons for doubting the syphilitic origin of the diffuse hypertrophic syphiloma of Fournier and that it is probable that future investigations will show this condition to be a rare manifestation of lymphogranuloma venereum.

A review of the literature shows that syphilis is rarely the chief etiologic factor in elephantiasis of the male genitalia. Undoubtedly, in many cases which have been reported as examples of syphilitic elephantiasis of the penis and scrotum the condition was in reality of lymphogranulomatous origin. In case 3 there was a strongly positive

Frei reaction and a history of venereal disease which was compatible with the diagnosis of lymphogranuloma venereum. Also, we were unable to demonstrate any other probable etiologic agents. This case was identical with the one reported by Barthels and Biberstein and others. The difference between the histologic changes in case 3 and in the cases reported by Barthels and Biberstein may be explained by the fact that the elephantiasis in our case had remained unchanged for seven years before a biopsy was performed. The virus in the scrotal tissue was in a latent state.

SUMMARY AND CONCLUSIONS

A critical review of the literature shows that syphilis is rarely the sole cause in elephantiasis. In many cases reported as examples of syphilitic elephantiasis, secondary streptococcic lymphangitis was probably the chief cause of the condition; in others the elephantiasis was coincidental with an existing syphilitic infection.

Two cases of the rare and almost forgotten syndrome described by Fournier under the title of diffuse hypertrophic syphiloma are reported.

The importance of syphilis and lymphogranuloma venereum as possible causes of elephantiasis of the lip and of the male genitalia is discussed.

A case of elephantiasis of the penis and scrotum in which the probable cause was lymphogranuloma venereum is reported.

ABSTRACT OF DISCUSSION

Dr. Harold N. Cole, Cleveland: I had the opportunity to see 1 of these patients. I think Trimble wrote something on the subject of elephantiasis of the lip in connection with syphilis. In regard to elephantiasis of the genitalia, in the past year or so I studied several more patients, and in 1 patient I was unable to prove the existence of lymphogranuloma venereum but was able to find Donovan bodies in the tissue; I therefore felt that the condition was probably granuloma inguinale. I am a little more conservative, therefore, about the theory that this type of elephantiasis is caused only by lymphogranuloma venereum.

Dr. E. W. Netherton, Cleveland: I had hoped to point out that there is a definite clinical similarity between the cases of elephantiasis of the lip of the type just discussed and those of elephantiasis of the genitalia. Some cases have been reported in which the elephantiasis of the genitalia preceded the elephantiasis of the lip. We believe that it is probable that future observations of thoroughly studied cases of elephantiasis of the face involving the eyelids and lips will show that in some cases of the type which have heretofore been thought of as syphilitic elephantiasis the elephantiasis is another manifestation of lymphogranuloma venereum.

A SIMPLIFIED COMPLEMENT FIXATION TECHNIC FOR THE DIAGNOSIS AND TREATMENT OF SYPHILIS

ITS SENSITIVITY AND SPECIFICITY

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Recently two of us[1] described a simplified complement fixation technic for syphilis, the advantages of which include reduction in time and labor, cost and technical errors. Without any loss of specificity, it showed an increased sensitivity over the routine Kolmer modification of the Wassermann test. Preliminary comparisons have also shown it to be more sensitive than the Kahn precipitation test, although less so than the Eagle test. It is now being used at the Graduate Hospital as one of three routine tests on all serums, the other two being the Kahn and the Eagle precipitation test.

A careful record of the results in a series of 1,500 tests (of both syphilitic and nonsyphilitic patients) has furnished us with additional data relative to its significance in the diagnosis of syphilis and the exclusion of syphilis both in patients from the syphilis service and in those admitted to the hospital at large. In all instances the Kahn and the Eagle test were performed on identical serums.

Any advance in the simplicity or sensitivity of the Wassermann test should be welcomed, as it is our feeling that for the diagnosis of syphilis a battery of three tests should be used when possible, with a complement fixation test as one of the three. When two tests are in disagreement,

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This research was aided by funds obtained from the Julia M. Keim Research Fund, University of Pennsylvania.

Read at the Sixty-Second Annual Meeting of the American Dermatological Association, Inc., Monte-Bello, Quebec, Canada, June 3, 1939.

1. Boerner, F., and Lukens, M.: (*a*) A Simplified Complement Fixation Technic for the Serologic Diagnosis of Syphilis, Am. J. Clin. Path. **9**:13, 1939; (*b*) A Study of the Sensitivity and Specificity of the Simplified Complement Fixation Test for Syphilis, to be published.

as happens not infrequently, the third test becomes of extreme usefulness, if only as a referee. In this report, we shall refer to our modification of the complement fixation test as the B-L modification.

TECHNIC

The technics of the Kahn and the Eagle test were outlined by their originators.[2] The B-L modification differs from the other modifications of the Wassermann test particularly in the mixing of certain of the reagents in bulk and the use of optimum doses of complement, hemolysin and antigen in place of units. Antigen and complement are combined and added as a single increment to the patient's serum, and then sensitized sheep cells are added. All reagents are used in smaller amounts, i. e., 0.1 cc. of serum is used, 0.5 cc. of antigen-complement and 0.5 cc. of sensitized cells. The total is but slightly over 1 cc. The amount of serum used, however, is really equal to or greater in relation to the reagents than the 0.2 cc. of serum that we have previously used in the Kolmer modification. Ice box fixation and

TABLE 1.—*Boerner-Lukens Modification of the Complement Fixation Test (Qualitative)*

	Serum, Cc.		Antigen-Complement Mixture, Cc.	Complement 1:30, Cc.		Sensitized Cells (0.75%), Cc.		Results
Tube 1	0.1	10 min.	0.5	...	15 to 18 hours	0.5	1 hour	
Tube 2	0.1	at 58 C.	...	0.5	at 8 to 10 C.,	0.5	at 37 C.	
Antigen control	0.1*		0.5	...	followed by 10 min. at 37 C.	0.5		Hemolysis
Complement control	...		...	0.5		0.5		Hemolysis
Corpuscle control	0.5†		...	...		0.5		No hemolysis

* Normal serum.
† Saline.

incubation of the mixture are essentially the same as in other modifications. Concerning the reagents and their titration, adjustment and preservation, detailed description has been given in a previous publication.[1a] Actually there are but three additions of reagents, the absence of any being readily detected by the difference in resultant volume. This makes for simplicity and ease of performance as well as of supervision. Although the volume is approximately one-third that used in the usual Wassermann test, the result is read with extreme ease in either Kolmer or Kahn tubes. The antigen used is prepared by a simplified method described by two of us in collaboration with Jones.[3] It is fortified with 0.4 per cent cholesterol, and its preparation requires but a few hours.

In this series, all reactions were read as positive, doubtful or negative, in accordance with the recommendations of the Committee on the Evaluation of Serologic Tests for Syphilis. In the complement fixation tests, only results usually

2. Kolmer, J. A., and Boerner, F.: Approved Laboratory Technic, ed. 2, New York, D. Appleton-Century Company, Inc., 1939.

3. Boerner, F.; Jones, C. A., and Lukens, M.: A Simplified Method for the Preparation of an Antigen for Use in the Complement Fixation Test for Syphilis, Am. J. Clin. Path. **9**:321, 1939.

denominated as 4 plus were called positive. Results of 3 plus, 2 plus, 1 plus and plus over minus were reported as doubtful, and complete hemolysis as negative. The Kahn test was reported according to the recommendation of Kahn; namely, a count over 6 as positive, from 2 to 5½ as doubtful and less than 2 as negative.

SENSITIVITY

From the data in table 2 it is apparent that the B-L modification of the Wassermann test is decidedly more sensitive than the Kahn test, but less sensitive than the Eagle test. These findings confirm a previous similar study by two of us.[1b] The proportionately larger number of doubtful Kahn tests is likely due to conservatism in the arbitrary division

TABLE 2.—*Results of Tests on 1,500 Serums*

B-L Modification		Kahn Test		Eagle Test	
Positive	396	Positive	148	Positive	148
		Doubtful	87	Positive	84
				Negative	3
		Negative	161	Positive	151
				Doubtful	1
				Negative	9
Doubtful	46	Positive	1	Positive	1
		Doubtful	15	Positive	14
				Doubtful	1
		Negative	30	Positive	23
				Negative	7
Negative	1,058	Positive	2	Positive	1
				Negative	1
		Doubtful	24	Positive	16
				Negative	8
		Negative	1,032	Positive	60
				Doubtful	1
				Negative	971

into positive and doubtful reaadings. This belief is supported by the fact that of 126 serums giving a doubtful Kahn reaction only 8 reacted negatively by both the B-L modification and the Eagle test. For the purpose of adequate comparison of the sensitivity of the tests, we believe that the positive and doubtful reactions should be grouped together. A doubftul reaction as interpreted by us usually is indicative of syphilis, except when it is refuted by the other two tests or is without confirmation on repetition.

SPECIFICITY

It was not possible to follow all cases in which the reaction was positive. Therefore, we directed our attention to those instances of positive B-L reactions associated with negative Kahn and Eagle reactions. It appeared reasonable that an analysis of this group would be most likely to reveal any false positive reactions. There were 9

cases in which such results were obtained and 4 of a positive reaction to the B-L test and a doubtful reaction to either the Eagle or the Kahn test. A résumé of these cases is given in table 3.

TABLE 3.—*Résumé of Thirteen Cases of "Positive" B-L Tests*

Case No.	Description of Patient: Race	Sex	Age	Diagnosis	Comment
	a. Nine Cases of "Negative" Kahn and Eagle Tests				
1, 2, 3, 4	.....	..	..	Under treatment for syphilis	
5	White	♂	33	Patchy atrophic gastritis	Still under study; subsequent Kahn and Eagle test "doubtful"
6	Negro	♀	46	Former thyrotoxicosis; present cholelithiasis	Dilated aorta; aortic second sound accentuated; test repeated with same result
7-8	.....	..	..	For blood bank	Impossible to follow up to date
9	.....	..	..	.....	False result, technical error
	b. Three Cases of "Doubtful" Kahn and "Negative" Eagle Tests				
10-11	.....	..	..	Under treatment for early syphilis	
12	.....	..	..	.....	Transient false positive
	c. One Case of "Negative" Kahn and "Doubtful" Eagle Tests				
13	.....	..	..	Under treatment for late syphilis	

Recapitulation: 7 patients under treatment; 1 patient suspected of syphilis; 3 patients incompletely studied, and 2 patients with false positive reactions

TABLE 4.—*Résumé of Seven Cases of "Doubtful" B-L Test with "Negative" Kahn and Eagle Tests*

Case No.	Description of Patient: Race	Sex	Age	Diagnosis	Comment
No. 1 with 3+	White	♂	53	Diabetes; lobar pneumonia	Febrile; light reflexes and deep tendon reflexes lost; serologic tests not repeated
No. 2 with 2+	Negro	♀	34	Pyonephritis	Febrile; sluggish pupils; serologic tests not repeated
No. 3 with 2+	White	♀	35	Rectal stricture; rectovaginal mass	Single serologic test; examination incomplete
No. 4 with 2+	Negro	♂	..	Treated syphilis	
No. 5 with 1+	White	♀	25	Chronic bronchitis	False doubtful reaction, technical error
No. 6 with 1+	White	♀	23	Lobar pneumonia	Febrile
No. 7 with ±	Negro	♂	56	Lumbar-sacral strain	Pupils unequal and sluggish to light; deep reflexes absent; further study needed

Recapitulation: 1 patient under treatment; 1 patient suspected of syphilis; 4 patients incompletely studied, and 1 patient with false doubtful reaction

There were 7 cases of doubtful positive reaction to the B-L test and negative reactions to both the Kahn and the Eagle test. A résumé of these cases is given in table 4.

In the 16 cases in which the B-L modification of the Wassermann test was the only one eliciting a reaction, there were 2 false positive

reactions, 1 false doubtful reaction and 7 reactions that could not be satisfactorily evaluated. At least 1 of the false positive reactions was discovered by retesting, and thereby a false report was avoided.

COMMENT

One is tempted to restate or formulate a sort of decalogue by which the physician should be guided. The truisms expressed are far from unique with us but deserve reemphasis, as confirmed by our experience and investigations:

1. For the routine serologic evaluation of syphilis at least two tests should be employed: one a complement fixation and the other a flocculation test. Ideally, three tests would be an improvement, the third acting in the capacity of referee.

2. A single positive report, even though all tests on the same serum give a strong positive reaction, should never be sufficient for the diagnosis of syphilis in the absence of clinical symptoms.

3. In the absence of clinical symptoms a positive reaction should be followed by a second test after a week.

4. All tests for routine diagnosis might well be reported as "positive," "doubtful" or "negative."

5. However, for patients to be treated or under treatment, the report of the test should indicate the degree of positivity.

6. A doubtful reaction to one test is more significant when accompanied with a positive reaction to the other or others and may be considered positive.

7. In all cases clinically early syphilis with positive serologic reports may be considered syphilis and treated immediately.

8. All serologic reports should indicate the tests employed and any modifications thereof.

9. A report of a negative serologic reaction (by any test) can never be taken as proving the absence of syphilis.

10. Reliance cannot be placed on serologic tests performed during an acute infectious or febrile stage of any disease.

SUMMARY AND CONCLUSION

We have described a new modification of the complement fixation test for syphilis, which has been determined to be more sensitive than the Kolmer modification and the Kahn flocculation test, although less so than the Eagle flocculation test. There has been no loss in specificity.

The Boerner-Lukens modification of the complement fixation test tends toward simplification through the use of an easily prepared

antigen and the addition of the reagents in combination. There ensues less labor and cost and the addition of improved supervision.

In a series of 1,500 tests, there were 20 instances of lack of accord in specificity, all of which are analyzed against the clinical status of the patient.

The continuance of the use of two or three tests for the serologic evaluation of syphilis is urgent.

A closer rapport is necessary between the serologist and the clinician, in order that the patient's interests may best be served.

EFFECT OF BISMUTH THERAPY ON LATENT PLUMBISM

PRELIMINARY REPORT

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In comparison with the arsenicals and mercurials employed in the treatment of syphilis, the bismuth preparations show a notably low toxicity. Stomatitis constitutes the only commonly encountered complication following the intramuscular injection of bismuth salts. Other reactions, including arterial and venous embolism, abscesses, arthralgia, jaundice, nephritis and cutaneous lesions, are rarely seen.

Stokes [1] listed such disturbances as abdominal cramps, diarrhea, polyneuritis, psychic symptoms and erythropoietic disturbances as following the administration of bismuth in the treatment of syphilis. These are also regularly noted in lead poisoning. This communication suggests that some of these reactions reported as being due to bismuth may actually have been the result of lead toxicity. Bismuth and lead are closely related chemical elements, and there is no reason why the toxicology of one should not resemble the toxicology of the other to a certain extent. However, latent plumbism is commonly encountered, especially in industrial centers, while bismuth toxemia is comparatively uncommon. The following case reports show that latent plumbism may become active after the injection of bismuth as an antisyphilitic agent.

REPORT OF CASES

CASE 1.—G. L. M., a 27 year old white man, was employed in a lead smelter in Idaho from January to June 1936. He stated that while he observed all possible precautions, such symptoms as abdominal and muscular cramps, discoloration of the gums, weakness and shortness of breath developed, and eventually he fainted while at work. The air in the smelter was said to have been saturated with lead dust. He was hospitalized in Kellogg, Idaho, for five weeks. A diagnosis of lead poisoning was made at this time. During the ensuing seven months he attempted to return to work on several occasions but each time suffered recurrences of the same symptoms. He finally abandoned the idea of continuing this line of employment. During his illness he lost 22 pounds (10 Kg.).

After this he was well until April 15, 1939, when a urethral discharge developed. This was diagnosed at a camp in California as gonorrhea and was treated accordingly. Early in June he noted four papular lesions on his penis, and a diagnosis of secondary syphilis was made and confirmed by serologic tests of the blood.

1. Stokes, J. H.: Modern Clinical Syphilology, ed. 2, Philadelphia, W. B. Saunders Company, 1934.

Antisyphilitic therapy was instituted at the camp by the simultaneous injection of 0.06 Gm. of mapharsen and 0.13 Gm. of bismuth subsalicylate. He received four injections of each within ten days. After this he was given three additional injections of each at weekly intervals.

The patient noted a recurrence of abdominal and muscular cramps, discoloration of the gums and weakness after the second treatment. These symptoms increased in severity after each subsequent injection. In addition, he lost 12 pounds (5.5 Kg.), in contradistinction to the gain in weight usually experienced by patients with early syphilis after the institution of therapy. His symptoms usually became aggravated twelve to twenty-four hours after the injections, although they were usually present constantly. He also complained of decreasing vision in his right eye. Examination revealed a typical lead line, consisting of pinpoint bluish black spots, less than 1 mm. from the gingival margin. The patient claimed that this had started only since the beginning of the injection therapy. The gums were not diffusely discolored as in bismuth pigmentation.

Bismuth therapy was discontinued, but the patient continued to receive intravenous injections of mapharsen. Within two weeks most of his symptoms, including the decrease in vision and the lead line, were greatly improved. Two weeks later he reported that he was entirely well.

CASE 2.—S. T., a 34 year old painter, stated that in September 1937 several lesions developed on his tongue and on his right thenar eminence. He visited a general practitioner, who found serologic evidence of syphilis in the patient and initiated therapy consisting of the intravenous injection of neoarsphenamine every five days. After twelve such treatments had been given, bismuth therapy was instituted.

After the first intragluteal injection, the patient suffered a sore hip and refused further treatments in this location. Therefore, he was given an injection of bismuth subsalicylate every five days in the left deltoid muscle. Soreness here did not inconvenience him at his work. In December 1937, after two or three such injections, the patient became very ill and was hospitalized. At this time he suffered severe abdominal cramps, pigmentation of the gums and other signs and symptoms leading to the diagnosis of lead poisoning. He remained in the hospital for about one month. After this, antisyphilitic therapy was resumed and he received 0.6 Gm. of neoarsphenamine every five days until I first saw him, on June 22, 1938.

Physical and laboratory examinations at this time gave completely negative results. He was given one injection of bismuth subsalicylate in the right hip, and because of a certain amount of soreness he refused further intragluteal therapy. As a result, the next two injections were administered into the left triceps muscle.

After the third treatment, the patient experienced severe abdominal cramps that he thought were like those he had suffered the previous December. Examination showed a number of discrete pinpoint pigmented spots on the side of the tongue about 1 mm. from the gingival margin. Bismuth therapy was immediately discontinued, but the patient continued to have severe intermittent abdominal pains for the following five weeks.

Since then he has received no further bismuth therapy, and there has been no recurrence of these signs or symptoms, despite his continuing to work as a painter.

COMMENT

Antisyphilitic therapy must be as nearly reactionless as possible to be successful. Not even financial considerations will lead to lapses in treatment as regularly as unpleasant paratherapeutic incidents. Con-

sideration of the cases reported here may explain some of the so-called "bismuth intolerances" and allow physicians to smooth the therapeutic road further.

It has been amply proved that lead is stored in the skeletal system of the body. In this location it is believed to be innocuous. However, when the stored metal is mobilized, or in other words when it is removed from the bones and taken into the circulation, a characteristic group of symptoms appear. This, of course, occurs when the amount of lead in the blood exceeds the concentration that the body can tolerate. These symptoms include pigmentation near the gingival margin, abdominal cramps, constipation or diarrhea, peripheral neuritis, anemia, stippling of the erythrocytes, encephalopathies and other derangements.

This mobilization may be accomplished in many ways. As simple a factor as an acid diet may be all that is necessary. Roentgenographic studies have shown that a lead line may be demonstrated near the epiphyses of growing children suffering from lead poisoning. A similar line has been found after bismuth therapy, and the consensus is that these lines are radiologically indistinguishable. This suggests that the two metals are stored in the same location. Fishback and Fishback [2] have demonstrated that after antisyphilitic therapy the greatest amount of mobile bismuth is found in the bones.

It is possible that the deposition of bismuth in the osseous system leads to the excretion of lead and explains the development of signs and symptoms of lead poisoning in such patients. These manifestations are dependent on the amount of lead in the circulation and not on the total amount present within the body.

A survey of the occupations in which the worker is exposed to lead suggests that latent plumbism must be common. According to Solis-Cohen and Githens [3] the exposed workers include painters, lead miners, lead workers, plumbers, type setters, dye workers, storage battery builders or repairers, enamelers, bullet makers, pottery glazers, paint manufacturers, solder handlers and gasoline (tetra-ethyl lead) handlers. Under these circumstances it is not surprising that bismuth therapy should occasionally cause activation of latent lead poisoning if the mechanisms suggested in this communication are correct.

The diagnosis of plumbism in these patients is based entirely on clinical evidence, but a careful consideration of the observations leaves little or no doubt as to its correctness. Both patients were exposed to lead. One was exposed during the treatments, and the other had had definite lead poisoning before receiving any bismuth therapy. One patient presented pinpoint pigmented spots on his tongue, which are

2. Fishback, H. R., and Fishback, D.: Experimental Studies of Long Continued Administration of Bismuth, J. Lab. & Clin. Med. **23**:127 (Nov.) 1937.

3. Solis-Cohen, S., and Githens, T. S.: Pharmacotherapeutics, Materia Medica and Drug Action, New York, D. Appleton and Company, 1928.

seen in lead poisoning but are of questionable occurrence in bismuth toxemia. The pigmentation of the gums was localized rather than diffuse, as commonly encountered after the injection of bismuth salts. The abdominal cramps experienced by these patients were much more severe than any personally observed as the result of administration of bismuth. Exactly the same symptoms developed in the first patient (case 1) after the injections of bismuth subsalicylate as those he had had during his previous attack of classic chronic lead poisoning. Case 2 was presented before the San Francisco Dermatological Society,[4] and the general tenor of the discussion was in agreement with the views expressed in this paper.

The second patient (case 2) was admittedly lax in removing the paint from his skin and clothes. This undoubtedly added to the amount of lead absorbed, increasing the need for storage space over the amount required by a cleanly worker. The daily ingestion of two quarts of milk was insufficient to prevent the development of manifestations of plumbism while this patient was receiving bismuth therapy. Since the cessation of injections of the bismuth compound he has been able to continue working as a painter without difficulty. Unfortunately neither patient was sufficiently cooperative to allow experimentation with various preparations, including bismuth and mercurials (orally administered), calcium, ascorbic acid and sodium thiosulfate.

This complication is apparently seldom recognized, as discussion of the matter with other dermatologists has failed to reveal a similar case. However, its potential importance is obvious when one considers the large number of patients who are constantly exposed to the noxious effects of lead. Therefore, it is suggested that the prophylactic treatment of lead poisoning in such workers as painters who are being given injections of bismuth preparations might further decrease the incidence of therapeutic complications in the treatment of syphilis.

SUMMARY

The cases of a painter and a smelter worker are presented. Signs and symptoms of lead poisoning in both patients followed the administration of bismuth in the treatment of a syphilitic infection.

It is suggested that bismuth may replace the lead stored in the bones and lead to the mobilization of lead, with the development of such symptoms as cramps and a lead line.

Prophylactic treatment of lead poisoning in those exposed to the influence of the metal may decrease the incidence of untoward reactions following bismuth therapy.

1624 Franklin Street.

4. Epstein, E.: Intolerance to Heavy Metal, Arch. Dermat. & Syph. **39**:570 (March) 1939.

LXXXVII.—CHROMOMYCOSIS OF THE FACE

REPORT OF A CASE AND A STUDY OF THE CAUSATIVE ORGANISM, PHIALOPHORA VERRUCOSA

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Chromomycosis (chromoblastomycosis), or dermatitis verrucosa, is a disease which has received little attention until recently, because of the small number of cases. Clinically it is a dermatitis usually of the extremities (hands or feet), which may be papular, nodular, verrucoid or granulomatous, with or without ulceration and abscess formation and usually yellowish brown. There has been no report of a systemic invasion, lymphangitis, pain or pruritus except in 1 case.[1] The microscopic picture may resemble that of tuberculosis, sporotrichosis, blastomycosis, syphilis, a granuloma or a foreign body reaction. However, brown thick-walled cells are seen in the tissue, probably chlamydospores, with intracellular wall formation and no budding. These structures are usually seen within the abscesses or giant cells.

The almost regular occurrence of the process on the extremities makes a lesion on any other part of the body seem unusual. With the exception of the first case reported in the United States by Lane [2] and by Medlar,[3] in which the lesions occurred on the buttock, and the one reported by Pedroso and Gomes [4] in Brazil, in which a lesion secondary

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Studies, observations and reports from the Departments of Dermatology and Mycology of the Barnard Free Skin and Cancer Hospital, service of Dr. M. F. Engman, Sr.

1. Carrión, A. L., and Koppisch, E.: Observations on Dermatomycosis in Puerto Rico: Report on a Case of Chromoblastomycosis, Puerto Rico J. Pub. Health & Trop. Med. **9**:169, 1933.

2. Lane, C. G.: A Cutaneous Disease Caused by a New Fungus (Phialophora Verrucosa), J. Cutan. Dis. **33**:840, 1915.

3. Medlar, E. M.: A Cutaneous Infection Caused by a New Fungus, Phialophora Verrucosa, with a Study of the Fungus, J. M. Research **32**:507, 1915; A New Fungus, Phialophora Verrucosa, Pathogenic for Man, Mycologia **7**:200, 1915.

4. Pedroso, A., and Gomes, J. M.: Sobre quatro casos de dermatite verrucosa produzida pela Phialophora verrucosa, Ann. paulist. de med. e cir. **11**:53, 1920.

to one on the foot occurred on the right side of the neck, there has been no record of a lesion of this disease elsewhere on the body. We are therefore reporting here a primary lesion of dermatitis verrucosa or chromomycosis on the face of a man 67 years old.

HISTORY OF THE DISEASE

Historically, the infection in man was perhaps noted for the first time by Pedroso, in 1911 at São Paulo, Brazil. At that time the investigator named the disease the "black blastomycosis," because he had observed brown or black cells in histologic sections of diseased tissue. Clinically the condition in certain aspects resembled blastomycosis. This case was not reported until 1920, when with Gomes he published reports of 4 cases. The fungi found in each case were named Phialophora verrucosa. In 1915 Lane and also Medlar in the United States published the first case of chromomycosis in this country, in which the lesion occurred on the buttock of a 19 year old boy. The organism was studied by Thaxter and named Phialophora verrucosa.

In 1922 Terra, Torres, da Fonseca and de Area Leão [5] studied a new case of dermatitis verrucosa, described the organism as Acrotheca pedrosoi and termed the disease "chromoblastomycosis" a blastomycosis produced by a colored fungus. Unfortunately, the name is still employed by many writers. Although the condition may simulate blastomycosis clinically, histologically it is not that disease, as has been pointed out by numerous investigators, especially by Wilson, Hulsey and Weidman.[6] The lesion may have the characters of several conditions or infections, such as tuberculosis, blastomycosis, coccidioidal granuloma, sporotrichosis, syphilis, a foreign body reaction and granuloma. There are seen in sections of diseased tissue, and occasionally in pus, brown thick-walled cells which may be unilocular or multilocular (fig. 2). These cells do not in any sense of the word resemble true blastomycetes, for they do not show typical budding. The name chromoblastomycosis has nothing to do with the biologic nature of the organism; it refers only to the color of the microbe in tissue. Accordingly, the name was changed to chromomycosis by Moore and Almeida.[7]

During the years from 1920 to the present time numerous cases of chromomycosis have been reported, with various fungi as causative

5. Terra, F.; Torres, M.; da Fonseca, O., and de Area Leão, A. E.: Novo typo de dermatite verrucosa, mycose por Acrotheca com associação de leishmaniose, Brasil-med. **2**:365, 1922.

6. Wilson, S. J.; Hulsey, S., and Weidman, F. D.: Chromoblastomycosis in Texas, Arch. Dermat. & Syph. **27**:107 (Jan.) 1933.

7. Moore, M., and de Almeida, F.: Etiologic Agents of Chromomycosis (Chromoblastomycosis of Terra, Torres, da Fonseca and Area Leão, 1922), of North and South America, Rev. biol. e hyg. **6**:94, 1935.

agents. Among the authors may be mentioned Mouchet and Van Nitsen,[8] who found a case in Rhodesia; Cavalcanti,[9] who in his thesis of 1924 at Rio de Janeiro described a case; Carini,[10] who in the same year reported 2 cases from São Paulo, and in 1927 Montpellier and Catanei,[11] who reported the disease from Algeria. Hoffman[12] in 1928 had a patient with this disease, and in the same year Bonne[13] published a case from Sumatra. In 1929 Borzone and Furno[14] noted the condition in Argentina, and a few years later Balina, Bosq, Negroni and Quiroga[15] described the first case from Buenos Aires. Several other cases were reported from northern Brazil, and Nauck[16] in 1931 described 2 more patients with chromomycosis from Rhodesia.

In January 1933 appeared the second case of chromomycosis in the United States in which the disease was due to P. verrucosa. This report, published by Wilson, Hulsey and Weidman,[6] is of interest chiefly because the infection occurred in a locality (Texas) widely separated from the region where the first case occurred (Boston) and secondly, because the lesion occurred on the foot. In the following year appeared the publication of MacKinnon[17] of the first case of chromomycosis in Uruguay, and in that case also the condition was due to P. verrucosa. This was the third case in which the disease was due to this organism and the

8. Mouchet, R., and Van Nitsen, R.: Sur une dermatite verruqueuse des noirs de la Rhodésie du Nord-Est, Ann. Soc. belge de méd. trop. **1**:235, 1920-1921.

9. de Mello Cavalcanti, J. T.: Contribução ao estudo das chromoblastomycoses, Thesis, Rio de Janeiro, 1924.

10. Carini, A.: Sur la dermatite verruqueuse, Bull. Soc. path. exot. **17**:227, 1924.

11. Montpellier, J., and Catanei, A.: Mycose humaine due à un champignon du genre "Hormodendron: H. algeriensis nov. sp.," Ann. de dermat. et syph. **8**:627, 1927.

12. Hoffman, W. H.: La cromoblastomicosis en Cuba y la enfermedad de guiteras o "chappa," Rev. méd. cubana **39**:420, 1928; Die Chromoblastomykose in Cuba, Arch. f. Schiffs- u. Tropen-Hyg. **32**:485, 1928.

13. Bonne, C.: Blastomycosis, with a Description of a Case of Chromatoblastomycosis from Sumatra, Geneesk. tijdschr. v. Nederl.-Indië **68**:705, 1928.

14. Borzone, R. A., and Furno, A.: Contribución al conocimiento de las blastomicosis americanas: Primera observación de dermatitis verrucosa en la Argentina, in Reunión de la Sociedad Argentina de Patología Regional del Norte (1929), Buenos Aires, 1930, vol. 1, pp. 351-356.

15. Balina, P. S.; Bosq, P.; Negroni, P., and Quiroga, M.: Un caso de cromboblastomicosis, autoctono de Argentina, Rev. argent. de dermatosif. **16**:369, 1932.

16. Nauck, E. G.: La importancia de las investigaciones histopatologicas para el diagnóstico de la dermatitis verrugosa (cromoblastomicosis), Rev. méd. german.-iber-am. **4**:671, 1931.

17. MacKinnon, J. E.: Estudio del primer caso uruguayo de cromoblastomicosis y "revista critica" sobre la enfermedad, Arch. urug. de med., cir. y especialid. **5**:201, 1934.

fourth in which the condition was caused by a Phialophora, since in 1 of the cases desecribed by Pedroso and Gomes the condition was found to have been caused by Phialophora macrospora.[18]

In 1933 a case of chromomycosis was reported by Carrión and Koppisch [1] in Puerto Rico, the first of several cases published by Carrión.[19] In the same year Martin, Baker and Conant [20] published from North Carolina the third case in the United States. Recent communication with de Almeida, of São Paulo, Brazil, has disclosed a number of additional cases from that region.

The case reported here is the fourth reported instance of this disease in the United States, the fourth in which the disease was due to P. verrucosa and the fifth in which it was due to a member of the genus Phialophora. It would be safe to say that chromomycosis as a disease is fairly well distributed over several continents, particularly North and South America and the interlying islands, that it is caused by several organisms [21] and that better clinical knowledge should reveal many more cases. Recent communication with Dr. F. W. Weidman, of Philadelphia, and with physicians in California has revealed additional cases.

REPORT OF CASE [22]

History.—M. S., a white man aged 67, of Creole-French descent, who was born in Missouri and had never been out of the state, presented himself in August 1938 at the Barnard Free Skin and Cancer Hospital, complaining of a lesion on the right cheek. The family history was irrelevant. The past medical history did not relate to his illness on admission. He had had no operations. At the age of 30 he suffered from stomach trouble due to lead fumes inhaled while working in a foundry. He had had typhoid fever at the age of 40 and had had malaria several times. There had never been symptoms referable to the cardiorespiratory system. For the past four years he had suffered from rheumatism of the back and extremities. There was no history of the ingestion of drugs.

His illness on admission had its beginning ten years previously, when he had burned his right cheek with the sulfur of a match. At that time he was engaged

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18. Moore, M., and de Almeida, F. P.: New Organisms of Chromomycosis, Ann. Missouri Botan. Garden **23**:543, 1936.

19. Carrión, A. L.: Chromoblastomycosis: Preliminary Report on a New Clinical Type of the Disease Caused by Hormodendrum Compactum, Nov. Sp., Puerto Rico J. Pub. Health & Trop. Med. **10**:543, 1935; Chromoblastomycosis: A New Clinical Type Caused by Hormodendrum Compactum, ibid. **11**:663, 1936.

20. Martin, D. S.; Baker, R. D., and Conant, N. F.: A Case of Verrucous Dermatitis Caused by Hormodendrum Pedrosoi (Chromoblastomycosis) in North Carolina, Am. J. Trop. Med. **16**:593, 1936.

21. Moore, M.: The Organisms of Chromomycosis of North and South America, Science **83**:603, 1936; Chromomycosis, Folia biol., 1936, nos. 61-65, pp. 266-269. Wilson, Hulsey and Weidman.[6] Moore and de Almeida.[18]

22. Case presented and discussed at the first annual meeting of the American Academy of Dermatology and Syphilology, held Nov. 14 and 15, 1939, at St. Louis (Arch. Dermat. & Syph. **40**:124 [July] 1939).

in loading and hauling wood and logs. The small burn healed slowly, and after healing a small spot appeared, which had gradually spread, over the ten year period, to the size noted when first seen.

Examination.—On admission it was noted that the patient was of swarthy complexion, with large and pitted sebaceous follicular openings on the face. On the right cheek was an irregular discrete elevated pinkish lesion, with the medial border impinging on the nasolabial fold. The surface was covered with a thin dry adherent scale and did not bleed when the scale was removed. The epidermis under the scale was thin and intact, with no ulceration and with several bluish pits on the surface. The lesion measured 4 by 5 cm., was elevated about 0.5 cm., and firm and had a pearly appearance, with the border merging into the normal skin.

The general physical examination revealed a presenile man who moved with difficulty because of arthritis. The ocular and general reflexes were normal. The oral mucosa was normal, including the area lying directly under the lesion on the cheek. The teeth were dirty and carious. The lungs were normally resonant with no rales. The apex of the heart was in the sixth interspace and the anterior axillary line. The heart was regular, with no murmurs, and the blood pressure was 180 systolic and 120 diastolic. The liver was neither tender nor palpable, and the spleen was faintly palpable. The tone of the anal sphincter was fair. The prostate was moderately firm and enlarged. The extremities were normal, and there was no dependent edema.

Laboratory Examination.—Urinalyses were normal. Results of blood sugar and sugar tolerance tests were within normal range. The nonprotein nitrogen content of the blood was 25 mg. per hundred cubic centimeters. Kahn reactions of the blood and spinal fluid were negative. On Sept. 10, 1938, the colloidal gold reaction of the spinal fluid was 4554444221. This may have been a laboratory error, as there were no symptoms or physical signs of any disease of the central nervous system. The albumin content and cell count of the fluid were normal, and a repetition of the colloidal gold test on another specimen six weeks later yielded a normal curve. Cultures of the spinal fluid gave negative results.

Roentgenograms of the skull were normal. The lungs showed normal pulmonary markings, but there were a moderate cardiac enlargement and diffuse dilatation of the aorta. The spine showed lipping and decided hypertrophic arthritic changes.

Histologic examination of the lesions revealed changes like those of granuloma, with marked infiltration with various cells and giant cells of the Langhans type, within some of which the typical dark brown, thick-walled, multilocular cells could be seen. The epidermis was greatly thickened. A diagnosis of chromomycosis was made. Because of the lack of exudative material, a second biopsy was made for culturing. The organism P. verrucosa was identified in the culture.

Progress.—To build up the iodide content, the patient was given mixed treatment, orally, for three weeks. The lesion regressed remarkably during this time, and his general condition and the arthritis so improved that he was able to walk without a cane. As he was to be presented to the clinic at the meeting of the American Academy of Dermatology and Syphilology in November 1938, he was given a placebo for the next six weeks. Since Nov. 15, 1938, he had been taking iodides by mouth, and the lesion was rapidly disappearing. The patient did not return for further investigation.

PATHOLOGY

Clinically the picture of chromomycosis may resemble one of several granulomatous lesions. In its early stages it may be confused with tuberculosis verrucosa cutis, epithelioma, blastomycosis, syphilis or

coccidioidal granuloma, in addition to various other granulomatous, mycotic infections. As the lesions progress in size, the hypertrophic changes appear definitely granulomatous, verruca-like, papular, nodular (some with pedicles) and psoriasiform and often showing ulceration and abscess formation. A crust may often be seen on the surface of the lesion, which offers no pain to the patient when it is removed, revealing a moist base, which on pressure may exude a mucoid, serous or purulent material within which may be found the brown, thick-walled, multilocular fungous cells.

The sites usually selected by the fungus are the feet (the dorsum and sides) extending up to and above the knees and the hands, with the lesions occurring on the dorsal region, involving the fingers and wrist and extending to and somewhat above the elbows. The case reported by Lane and Medlar was an exception, as is the case reported here.

To date there has been little or no indication of pain or itching in the affected parts. There seems to be no lymphangitis or lymphangitic metastasis. The case of Carrión and Koppisch [1] seems to be an exception in that these authors stated the belief that a metastasis occurred to the forearm.

The microscopic changes observed in the tissue suggest one of the diseases previously mentioned, particularly tuberculosis. However, a number of points of difference can be distinguished in addition to the finding of the typical fungi, which at once suggest a diagnosis of chromomycosis. The epidermis shows a decided hyperkeratosis and acanthosis due to the hyperplastic changes in the epidermal cells, which result in the thickening, broadening and elongation of the interpapillary pegs. There can also be observed a certain grade of parakeratosis.

The corium, however, shows a decided change, with intense infiltration, edema and fibrosis. Discrete granulomatous lesions are observed, showing central areas of polymorphonuclear leukocytes in various stages of degeneration, numerous lymphocytes, plasma cells, eosinophils, Russell's fuchsin bodies, epithelioid cells, macrophages, fibroblastic changes, discrete microabscesses and giant cells of the Langhans or foreign body type arranged in tubercle-like fashion (fig. 1). Within these giant cells or in the abscesses the sclerotic cells of the fungus can easily be seen, either as single cells or grouped in clusters. The picture is so similar to that of tuberculosis, as has also been pointed out by Wilson, Hulsey and Weidman, that except for the presence of P. verrucosa it is somewhat difficult to distinguish it from this disease.

DESCRIPTION OF THE ORGANISM

In tissue, as has been pointed out before, the large sclerotic cells of the fungus are dark brown, thick walled, spherical or irregular, and

single or multiple; they reproduce by enlargement and cross wall formation, to form mulberry-like clusters, and never by budding. Occasionally one may be misled by a picture as seen in figure 2. In actively infected tissue these are the only forms noted. In old necrotic tissue there may be seen occasionally a germination of the cells to form short filaments, somewhat similar to those seen in figure 3 *1*, where the tissue has been inoculated on artificial mediums.

Since we were unable to express any fluid or exudate from the tissue, a biopsy specimen was taken, and the material was cut up into fine pieces aseptically and inoculated into fresh Sabouraud's maltose and Czapek's

Fig. 1.—Histologic section of chromomycosis. Note the tuberculoid reaction with giant cells. Hematoxylin and eosin stain (× 107).

agar. Approximately six days after insemination small black colonies, the size of a pinhead, could be noticed on Czapek's medium. Several of the inoculated bits of tissue were then taken from the artificial medium, fixed in solution of formaldehyde, embedded in paraffin, sectioned and studied. The fungous cells developed, as seen in figure 3, first by an elongation of the cells and then by the sending out of irregular prolongations, which eventually became of somewhat uniform size, with cross wall production to form the type of mycelium seen on artificial substrates. Colonies developed on the Sabouraud maltose agar approximately eleven days after insemination. When the colonies grew to a suitable size, subcultures were made on various mediums in order to

study the morphologic picture produced, so that the genus and species might be determined.

The development of the fungus on artificial mediums with the resulting morphologic changes have been considered by several writers. The essential features, however, may be repeated here for the sake of completeness. The strain of P. verrucosa isolated in the case described here is essentially similar microscopically to those found in the cases reported from Boston, Texas and Uruguay.

When first isolated on artificial substrates, the thick-walled brown cells seen in sections germinate to form multiseptate filaments, which

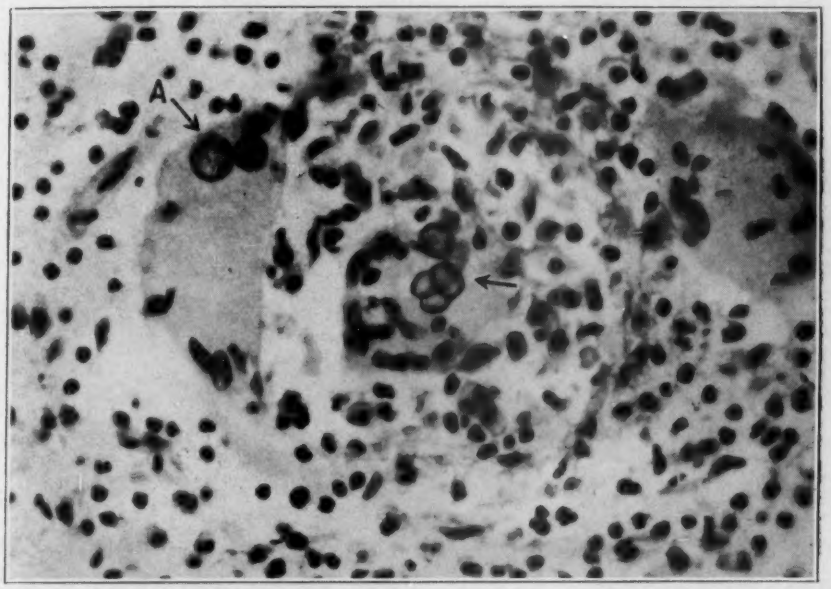

Fig. 2.—Tissue section. Note sclerotic, dark, thick-walled cells in giant cells. Hematoxylin and eosin stain (× 500).

vary from approximately 2 to 5 microns in diameter. On some mediums, such as Czapek's or malt extract agar, these hyphae are of smaller diameter than on substrates having more peptone as a constituent. The hyphae, or filaments, are seen in culture either as isolated strands or in bundles (coremioid). This is particularly apparent in the compactly growing colonies.

On such mediums as peptone agar (fig. 3*2*) the filaments occur in the form of chains of cells, or what is commonly referred to as a moniliform growth. Among these cells there may also be seen larger, thick-walled forms, which seem to correspond to those seen in tissue. On Loeffler's agar these forms are more apparent and simulate more

closely the parasitic structures. The moniliform development, however, makes up only part of the culture, since on a medium such as Sabouraud's dextrose or maltose agar there are seen also the multiseptate

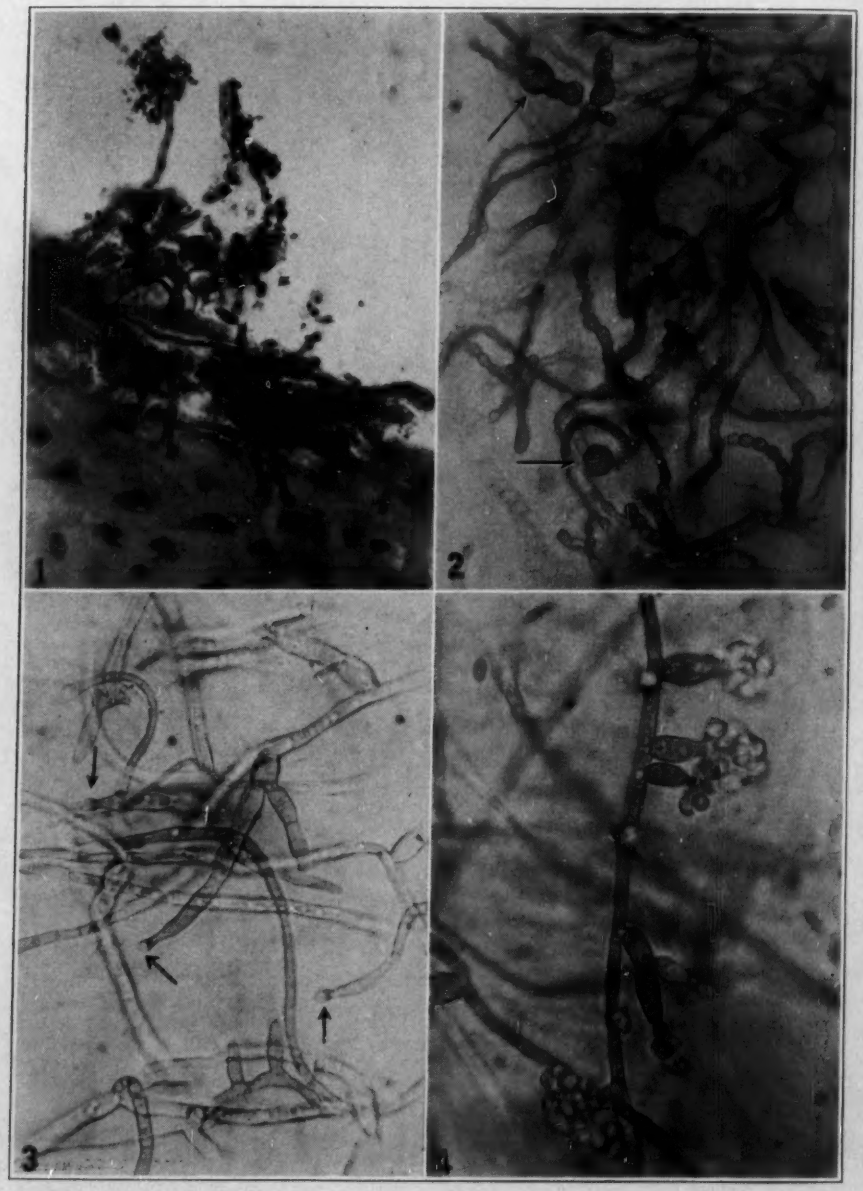

Fig. 3.—*1*, germinating sclerotic cells in tissue; hematoxylin and eosin stain (× 335); *2*, monilioid and chlamydosporic cells on peptone agar (× 335); *3*, early development of phialides on Sabouraud's maltose agar (× 335); *4*, phialides showing conidia held together by gloea on Czapek's agar (× 335).

filaments seen in figure 3*3*. The latter hyphae then serve as the progenitors of the phialides and conidia, or phialospores, which characterize Phialophora.

The phialides, or cup-bearing endogenous spore formers, vary somewhat on the different mediums, but they attain their greatest number and largest variety of forms on Czapek's medium (fig. 3*4*). These spore-bearing structures may be single or many celled, simple or branched, elongate or short, and terminal, lateral or alternate on a hypha. Just as the phialides may be of diverse forms, so do the spores vary in shape and dimensions. They vary from small, spherical cells, approximately 2 microns in diameter, to ovoid or somewhat fusiform conidia, measuring approximately 1 to 3 by 2 to 4 microns. The conidia are usually seen as groups at the mouth of a phialide, held together more or less by a mucilaginous material termed gloea (fig. 3*4*). The conidia are then capable of germinating to form again the structures already mentioned.

Cultural Description.—The strain of P. verrucosa isolated from the case reported here showed the following characteristics on various mediums:

Czapek's Agar (p_H 4.3) (fig. 4*5*).—The fungus showed the most rapid growth on this medium, attaining a diameter of 4.3 cm. after twenty-two days, with a penetration of the substratum. The colony was blue-black to ochraceous brown at the periphery. The central mycelium in the form of a button was aerial and rat gray. The filaments were 2 to 5 microns in diameter, brown, thick walled and multiseptate, showing moniliform development. The conidia were 1.5 to 2 by 2 to 4 microns, with many unicelled to multicelled, simple or branched phialides.

Sabouraud's Dextrose Agar (p_H 5.6).—Growth was fairly rapid, the colony measuring 3.5 cm. in diameter after twenty days, showing little growth downward, with a sharply defined periphery. The color was slate gray to black for the aerial tufted mycelium, becoming olivaceous gray peripherally with some color diffusion into the agar. The filaments were 2 to 3 microns in diameter, light brown, and thin walled, with few cross walls. The conidia varied in size, measuring 1 to 3 by 1 to 4 microns, with many of them spherical, but mostly ovoid. The phialides were present in varying proportions and number.

Sabouraud's Maltose Agar (p_H 5.6) (fig. 4*7*).—Growth was at the same rate as on the dextrose medium, attaining a diameter of approximately 3.7 cm. after twenty days. The features were essentially similar to those on the dextrose medium.

Potato-Dextrose Agar (p_H 5.9) (fig. 4*6*).—The colony was 3.3 cm. in diameter after twenty days. The culture was dark olivaceous gray. The aerial growth was more or less felted, with a central button, and was light olivaceous gray. The hyphae measured 3 to 4 microns in diameter, were dark brown and thick walled and showed many cross walls. The conidia measured 1.5 to 2 by 2 to 4 microns. The phialides were few, 4 to 5 by 7 to 11 microns. There were seen also a number of spherical, thick-walled cells, 6 microns in diameter.

Yeast-Dextrose Agar (*Difco Product*, p_H 7.0) (fig. 4*8*).—The colony was 3.2 cm. in diameter after twenty days' growth. The color of the moist periphery

was black with the aerial, centrally tufted mycelium dark gray. The filaments were 2 to 4 microns in diameter and multiseptate. The conidia measured 1 to 2 by 2 to 4 microns, and there were few phialides. Spherical thick-walled cells were 4 to 6 microns in diameter.

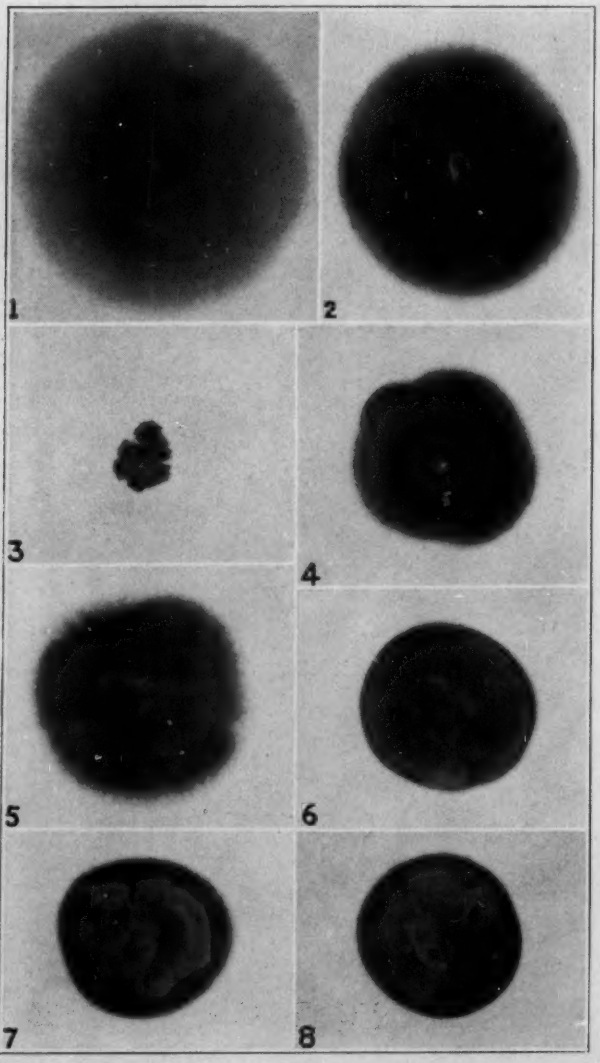

Fig. 4.—Cultures of Phialophora, four-fifths actual size: *1*, P. verrucosa (Boston case) on Czapek's agar; *2*, P. macrospora (São Paulo case) on Czapek's agar; *3*, P. verrucosa (Texas case) on Czapek's agar; *4*, P. verrucosa (Uruguay case) on Czapek's agar; *5*, *6*, *7* and *8*, P. verrucosa (St. Louis case) on Czapek's agar, potato-dextrose agar, Sabouraud's maltose agar and yeast-dextrose agar, respectively.

Glycerin Agar (p_H 7.0).—The glycerin agar cultures were highly distinctive in being decidedly raised above the surface of the medium and intense black, with the aerial hyphae showing a dark gray. The periphery was sharply defined and somewhat moist and shiny. The diameter of the colony was approximately 3 to 2 cm. after twenty days.

COMMENT

As a result of the relative infrequency of chromomycosis, it has not been possible for clinicians to determine the many clinical pictures that this disease exhibits. The finding of a lesion in an unusual location is therefore worthy of report. In spite of the fact that a large number of fungi may be involved as the incitants,[23] the macroscopic appearance of the lesion is essentially alike for all the microbes. The question of portal of entry or mode of infection was brought up by Wilson, Hulsey and Weidman. The disease is noted particularly in patients that have at one time or another been active in some type of rural work. The history usually shows that the lesion has developed after some trauma, no matter how slight. The chief sites have been the extremities. The lesion may be explained on the basis, therefore, that the organism is a saprophyte, growing on dead or decaying logs, as Conant [24] has attempted to show, and that the extremities are more subject to trauma and subsequent contact with the fungus in the natural habitat. This explanation serves possibly to elucidate the manner of infection in the patient described here, since he had traumatized his skin by burning and had been actively engaged in hauling and handling logs and lumber.

The confusing of chromomycosis with other mycotic infections, such as blastomycosis or coccidioidal granuloma, and with tuberculosis verrucosa cutis is not difficult to understand. Clinically there certainly is little, at times, to differentiate one disease from the other. They are all granulomatous. Mycotic granulomas more or less affect the skin in the same manner. The histologic picture is essentially similar except perhaps for the intensity of reaction and the development of the lesion in certain patients, dependent on the rapidity of reproduction and spread of the fungi in tissue. The organisms producing these diseases do not seem to liberate an exotoxin in the true sense of the word, but do their damage perhaps as actively proliferating foreign bodies. They are therefore not to be strictly compared with the typical granulomas produced by inanimate foreign substances, in which the foreign material remains localized, unless it is soluble in the skin, and eventually becomes more or less walled off from the rest of the tissue.

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23. Wilson, Hulsey and Weidman.[6] Moore and de Almeida.[18] Martin, Baker and Conant.[20]

24. Conant, N. F.: The Occurrence of a Human Pathogenic Fungus as a Saprophyte in Nature, Mycologia **29**:597, 1937.

It is also curious to realize that of the 3 cases previously reported in which the condition was due to Phialophora verrucosa, in the first the lesion was on the buttock; in the second the foot was involved, and in the third there was an infection of the hand. In the fourth case reported here the face was involved.

A comparison of the several strains of Phialophora is interesting. The first culture isolated, that from Boston (fig. 4 *1*), showed the greatest amount of growth. This possibly was because it had been growing on artificial mediums for the longest period. P. macrospora, isolated in Brazil (fig. 4 *2*), showed similar cultural characteristics but differed in the size of conidia or spores. The strain of P. verrucosa isolated in Texas (fig. 4 *3*) varied considerably macroscopically from all other strains in that it grew very slowly, attaining a diameter in twenty days which was approximately one-fifth that of the other cultures. The rate of development increased somewhat after this period, but the organism did not attain the magnitude of growth seen in the other strains. The organism from Uruguay (fig. 4 *4*) and that from St. Louis (fig. 4 *5, 6, 7, 8*) showed a similar rate of development but had some slight differences in gross appearance. It seems, therefore, that in spite of the fact that all the strains of P. verrucosa from different localities were identical microscopically, they differed macroscopically and somewhat physiologically. This is in addition to the clinical observation that each affected a different part of the body.

SUMMARY AND CONCLUSIONS

The case of a 67 year old man with chromomycosis of the face for approximately ten years due to Phialophora verrucosa is presented. The location of the lesion was unusual, this being the first case, as far as we know, in which the face was a primary focus of infection following a trauma due to a burn with the sulfur of a match. It is also of interest that the patient acquired the infection in Missouri and had never been out of the state.

The lesion grossly simulated blastomycosis or tuberculosis verrucosa cutis. The diagnosis was made by finding the thick-walled, brown multilocular cells in the tissue and was subsequently confirmed by the isolation in culture of P. verrucosa. Although in culture the various strains of P. verrucosa from Boston, Texas, Uruguay and St. Louis are identical microscopically, they differ somewhat macroscopically. The Texas strain is decidedly slow in evolution.

P. verrucosa is described in culture, both macroscopically and microscopically. The granulomatous features of the histologic picture of this disease are discussed.

PERIPHLEBITIS NODULARIS NECROTISANS

AN ATTEMPT AT DEFINITION AND CLASSIFICATION

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NEW YORK

One of the great faults of dermatologic nomenclature is the haste with which a new name is coined to designate anomalous symptoms of a previously well established clinical entity. To make matters even worse, the needless confusion which thereby ensues in the literature is kept up for years by the continued use of a name which in all common sense should have been relegated to limbo shortly after its conception. This holds particularly true of the term periphlebitis nodularis necrotisans, which was first introduced by Philippson [1] in 1901. While the term has rarely appeared in the literature, it has done so frequently enough to warrant an analysis of the evidence pro and con to determine whether it is a clinical entity. I believe that I can offer sufficient evidence to prove conclusively that it has no claim as an original dermatosis, and that it is either an aberrant form of Bazin's disease or a tuberculid.

The symptoms of periphlebitis nodularis necrotisans are fairly constant, and my personal observation of this condition is probably confined to a dozen or more cases. In the large majority of these there were on the legs, and almost invariably in the usual location of Bazin's disease, a variable number of subcutaneous nodules, arranged in beadlike or linear formation. These nodules varied greatly in size, were sometimes painful on pressure and were usually pink to violaceous. At times there seemed to be no inflammatory changes in the overlying skin. As time went on the nodules became harder and darker and then shrank in size and eventually disappeared, leaving a brownish pigmented stain with some retraction or dimpling of the skin. Rather infrequently the nodules broke down and ulcerated and when they did they could not be distinguished clinically from Bazin's disease. More rarely the patient presented a series of twenty-five or more pea-sized violaceous nodules, which were painful and tender on palpation. Many of these nodules presented

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Read at the Sixty-Second Annual Meeting of the American Dermatological Association, Inc., Monte-Bello, Quebec, Canada, June 2, 1939.

1. Philippson, L.: Ueber Phlebitis nodularis necrotisans (Beitrag zu dem Studium der Tuberculides von Darier), Arch. f. Dermat. u. Syph. **55**:215, 1901.

superficial erosions, and others ulcerated. In the latter eventuality, the lesions sometimes spread over the legs laterally and anteriorly as well as posteriorly. In a considerable number of the cases that I have observed the subcutaneous nodules of periphlebitis nodularis necrotisans appeared concomitantly with typical lesions of erythema induratum, and—what is of great importance—they disappeared under the orthodox treatment of Bazin's disease in exactly the same manner and time as the typical lesions of that well known entity. Again, when the two types of lesions were present, I have noted that small and new nodules have not progressed but have healed entirely at the same time that the larger typical lesions of erythema induratum resolved.

The differential diagnosis of periphlebitis nodularis necrotisans and periarteritis nodosa is not usually difficult. In the former disease the lesions are located on the legs only, with no constitutional symptoms, and the nodules and ulcers are not associated with other cutaneous changes. In periarteritis nodosa there are, besides the nodular lesions, occasional swelling and pain in the joints, elevation in temperature, cutaneous hemorrhagic spots, urticarial efflorescences and polymorphous erythema. Nodules occur on the arms as frequently as on the legs. Vascular involvement of the arms closely resembling livedo racemosa has been reported by Carol and Prakken.[2]

The histologic picture of periphlebitis nodularis necrotisans is interesting. The proponents of the theory that the condition is an entity from the histologic point of view have frequently cited Philippson, yet a careful perusal of his paper shows that while he definitely stated that the most common histologic observations in his first case were partial or complete necrotization of the venous walls and their contents in the subcutis and a leukocytic infiltration within the vessel walls in the cutis, and that there seemed to be no interrelation microscopically with tuberculosis in that particular nodule, he did succeed in demonstrating the tubercle bacillus in two other nodules and in producing tuberculosis by inoculating the eye of a rabbit with a fragment of one of them. This to my mind proves that the eruption in Philippson's case was definitely tuberculous. Even Philippson himself was convinced that the appearance of the lesions in his case resembled the description of tuberculids by Darier in 1896, and he so stated in the opening paragraph of his paper. There is no doubt that the histologic picture of destruction of the veins by necrotic degeneration of their walls with no evidence of tuberculosis occurs in a number of specimens while an equal, if not a greater, number show tubercles and the other characteristic changes of tuberculosis. Why does this discrepancy occur? I believe that it can be

2. Carol, W. L. L., and Prakken, J. R.: Die kutane Form der Periarteritis nodosa, Acta dermat.-venereol. **18**:102 (Feb.) 1937.

best explained in the words of the late Walter Highman [3] before the Section of Dermatology and Syphilology of the New York Academy of Medicine, on March 4, 1930:

> Because . . . [the histologic picture of erythema induratum did not appear] in the lesion examined in this patient does not prove that it would not be found in another lesion. I think in this discussion we have the pseudophilosophy Molière referred to in his play . . . "Les precieuses ridicules." . . .
>
> If you take one lesion from a patient with erythema induratum, Bazin, you might find the structure of tuberculosis and of an ordinary inflammation in the same specimen, indeed in the same section. That is so typical of all tuberculosis. In cases that are clinically erythema induratum, Bazin, you may find tuberculous structures in some and not in others.

To my mind, Highman was right in his statement; it might well be that the apparent discrepancies in histologic work would greatly diminish if two, three or even more different biopsy specimens were taken in the same case instead of a large number of serial sections from a single piece of tissue. I have not infrequently observed a complete reversal of a histologic report after the examination of a second or even a third specimen.

Let me now consider the opinions of various American dermatologists as to the entity of this condition. A case of periphlebitis nodularis necrotisans was presented by Eller [4] before the New York Dermatological Society on May 15, 1928. The patient, a woman aged 24, stated that the eruption had been present for two years. On the lower extremities there were many reddish elevations, some showing a tendency to linear formation. There was no histologic report. Drs. G. M. MacKee and H. H. Whitehouse made a diagnosis of Bazin's disease. Dr. Highman said:

> Why call it periphlebitis nodularis necroticans? Bazin's disease is a perivascular infiltration, and for a good reason. The infiltration cannot escape blood vessels. In fact, a characteristic feature of Bazin's disease is the relation of the infiltration to blood vessels. A name like this is another example of complicating dermatology in the most fatuous manner possible. It is unjustifiable by fact or necessity.

A case of periphlebitis nodularis necrotisans was presented by MacKee [5] before the New York Dermatological Society on Jan. 28, 1930. The patient was a man aged 20. The eruption consisted of deep-seated hard and slightly painful nodules. Most of them ulcerated, and the ulcers lasted for many months before healing. The eruption was of

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3. Highman, W., in discussion on Eller, J. J.: Periphlebitis Nodularis Necroticans, Arch. Dermat. & Syph. **22**:722 (Oct.) 1930.

4. Eller, J. J.: Periphlebitis Nodularis Necroticans, Arch. Dermat. & Syph. **19**:138 (Jan.) 1929.

5. MacKee, G. M.: Periphlebitis Nodularis Necrotisans, Arch. Dermat. & Syph. **22**:367 (Aug.) 1930.

two years' duration. Under the microscope there was a dense infiltration of round cells in the lower part of the cutis, but mostly in the fat and around thickened blood vessels. Giant and epithelioid cells were absent. There were a few plasma cells. The case was presented as one of periphlebitis nodularis necrotisans with the understanding that this condition was an aberrant form of Bazin's disease. In the discussion Drs. Wise, J. F. Fraser, E. R. Maloney and Highman made a diagnosis of Bazin's disease. The same patient was shown by Wise [6] before the Manhattan Dermatological Society, on Feb. 11, 1930. A patient was presented by me [7] before the New York Academy of Medicine, Section of Dermatology and Syphilis, on Nov. 8, 1933, with the diagnosis of periphlebitis nodularis necrotisans. The patient was a man aged 40. He presented a number of indolent violaceous red nodular lesions on the legs, some of which had necrosed and broken down to form shallow ulcers. They had been present for four months. The histologic report was of a nondescript picture. Roentgenograms of the chest showed an infiltrated shadow in the apex of the left lung. The shadow was fairly sharp and was typical of tuberculosis. In the discussion Dr. M. B. Sulzberger stated:

> It would be best to drop such terms as "periphlebits nodularis necroticans" and "dermatitis necrotica" in the designation of ulcerative processes on the lower legs such as that in Dr. Bechet's case. Philippson, who applied the latter term to two similar cases, later read Darier's description of papulonecrotic tuberculids. He then recognized the resemblance between Darier's tuberculids and the condition in his cases and fortunately had the opportunity to reexamine the patients. After a long and tedious investigation he was able to prove histologically and by animal inoculation that the condition in both of his cases was tuberculous. . . . For this reason, it is now generally accepted that these terms, as well as "hydro-adenitis suppurativa," which Pollitzer was the first to use for a picture clinically somewhat similar, are merely old names used before the tuberculous etiology of this entity was recognized. . . . In the vast majority of cases of this nature the lesions can be proved to be tuberculids provided one takes sufficient time and pains and has the opportunity to study a sufficient number of lesions histologically by the injection of tuberculin, and by guinea-pig inoculation.

Dr. Sigmund Pollitzer said:

> Dr. Sulzberger has already referred to Philippson's work. The cases that he described were identical, and histologic examination showed the same picture that I had found a year or two earlier and reported under the name of "hydro-adenitis suppurativa." Philippson and I corresponded later on the subject and agreed on the essential features. Five or six years later Darier established the group of the tuberculids. Both Philippson's term and mine have been eliminated by the increase in knowledge, and I see no reason for reviving them.

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6. Wise, F.: Periphlebitis Nodularis Necrotisans, Arch. Dermat. & Syph. **22**:546 (Sept.) 1930.

7. Bechet, P. E.: Periphlebitis Nodularis Necroticans, Arch. Dermat. & Syph. **29**:753 (May) 1934.

SUMMARY

Clinical, and to a certain extent, laboratory, evidence indicates that periphlebitis nodularis necrotisans is not a clinical entity but an aberrant form of Bazin's disease or, less likely, a member of the large group of papulonecrotic tuberculids. This has been proved, first, by the testimony of Philippson, the originator of the name, who besides admitting the similarity of the syndrome to tuberculosis of the skin, succeeded in finding the tubercle bacillus in the nodules and in producing tuberculosis by inoculating a rabbit with a fragment of one of them; second, by the frequency with which I have observed the concomitant appearance of the subcutaneous nodules of so-called periphlebitis nodularis necroticans and of the typical lesions of erythema induratum, and the simultaneous healing of both types of lesions under the usual therapy of erythema induratum; third, by the almost unanimous opinion of American dermatologists that periphlebitis nodularis necrotisans is an aberrant form of erythema induratum of Bazin and not a clinical entity, and fourth, by the testimony of such excellent histologists as the late Drs. Pollitzer and Highman to the effect that despite the conflicting histologic reports the term periphlebitis nodularis necrotisans should be dropped and the syndrome hitherto described under that name classed as a tuberculoid or tuberculous dermatologic manifestation.

In conclusion, I hope that my effort to prove the nonexistence of a dermatosis with another long name may be successful, thereby simplifying to a slight degree the still formidable and occasionally unjustifiable nomenclature.

ABSTRACT OF DISCUSSION

Dr. Harold N. Cole, Cleveland: Perhaps a little more difficulty is encountered in the treatment of erythema induratum in Cleveland than in New York, but I should like to know what new type of treatment it is that gives such uniform and good results.

Dr. Marion B. Sulzberger, New York: Dermatologists must agree today with Brocq's idea of *réaction cutanée* in regard to many of the morphologic entities. For example, in nodose erythemas, in multiform erythemas, in sarcoid reactions and in similar conditions it has been proved that closely similar or almost identical clinical and microscopic pictures can be produced by different etiologic agents. It would be tempting to say that the same remark may apply to those conditions of the legs diagnosed as erythema induratum or papulonecrotic tuberculid and that they too may have a different cause in different cases. Unfortunately, this has never been proved to be true. It does not seem that any typical case has ever been proved due to any etiologic agent other than the tubercle bacillus. Thus, a case of nodose erythema may be caused by a streptococcus, by the lepra bacillus, by the virus of lymphogranuloma venereum, by a drug such as bromide or iodide or salicylate and by any one of many other etiologic agents. However, there are no authenticated and well studied cases of Bazin's disease with the typical clinical picture and histologic changes and no case of typical papulonecrotic tuberculid in which causation by an agent other than the tubercle

bacillus has been proved. All typical cases in which extensive, thorough and proper examinations have been made have been shown to be of undiscoverable cause or have eventually been shown to be of tuberculous origin. In these etiologic examinations, the determination of macroscopic or microscopic changes must necessarily play a minor role. For since one starts by granting the premise that identical or similar cutaneous changes may be the result of different causes, one can obviously draw no binding conclusion as to causation by means of mere morphologic analysis. In determining the cause of these cutaneous pictures, one must go beyond morphologic factors and consider epidemiologic ones, immunologic reactions and particularly bacteriologic investigations. Proper bacteriologic investigation of a cutaneous lesion suspected of being a tuberculid may have to consist of many biopsies of abundant tissue from various lesions in different stages of development and involution and numerous animal inoculations with this material. It is sometimes necessary to inoculate as many as ten guinea pigs from each specimen of tissue, and all the animals should be allowed to live until one is certain that tuberculosis will not develop in some one of them. Wherever one has been fortunate enough to have facilities for such studies, it has eventually been shown that in typical cases of Bazin's disease and papulonecrotic tuberculids tubercle bacilli are usually present, regardless of whether the histologic morphe presents banal perivasculitis or tubercle structures. In this manner, the lesions in Phillipson's own cases of "periphlebitis nodularis necroticans" were shown to be tuberculids, and Phillipson himself published this fact and withdrew his descriptive term in favor of Darier's etiologic designation.

DR. PAUL E. BECHET, New York: In response to Dr. Cole's question as to what constitutes the orthodox treatment of erythema induratum, I beg to state that I consider aurotherapy, roentgen irradiation, the injection of tuberculin and a high vitamin intake as the routine or orthodox treatment. Of all these remedies, I have found that the use of gold compounds and roentgen irradiation have given me the best results, and I may be drawing a withering fire on myself by stating that I have even observed several cures by means of their use. At the same time, I do not wish to convey the idea that I believe these remedies are specific, as they not infrequently dismally fail. I am sorry that Dr. Cole misconstrued the definition of the word "orthodox," which means "in accordance with sound doctrine." Such a definition certainly does not convey the idea of infallibility. I feel sure that erythema induratum is just as successfully or as unsuccessfully treated in Cleveland as in New York, and I hope that Dr. Cole's delusions about the superiority of New York therapy will not become chronic.

BULLOUS ERUPTION FOLLOWING SULFANILAMIDE THERAPY

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The expansion of the therapeutic application of sulfanilamide has been more or less paralleled by the recognition of apparently new toxic reactions to the drug. Loveman and Simon [1] recently reported a case of bullous stomatitis in which a single bullous lesion developed on the hand as a result of sulfanilamide therapy. Because of the limitation of the eruption, pemphigus was not suggested clinically, although it obviously might have been so considered had similar lesions occurred over a more widespread area of the body. Small vesicular lesions have been noted in sulfanilamide eruptions by Menville and Archinard [2] and by Tedder.[3]

Since the introduction of sulfanilamide as an agent in the treatment of pemphigus by Caro,[4] conflicting opinions regarding its worth have been expressed.[5] It is interesting that sulfanilamide may lead to the development of tense bullae on apparently normal skin, in association with definite constitutional symptoms.

REPORT OF A CASE

O. N., a 54 year old white man, fell on July 5, 1939, bruising and lacerating his left hand. On the following day his hand began to swell, and there were marked pain and tenderness. He entered the hospital on July 7, and a diagnosis of acute cellulitis of the left hand with palmar space infection was made. Sulfanilamide was administered orally, and he made a prompt recovery, being discharged on July 13. During his stay in the hospital he received 20 grains (1.3 Gm.) of the drug four times a day, administered with an equal amount of sodium bicarbonate. A total of 400 grains (26 Gm.) of sulfanilamide was ingested.

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1. Loveman, A. B., and Simon, F. A.: Fixed Eruption and Stomatitis Due to Sulfanilamide, Arch. Dermat. & Syph. **40**:29 (July) 1939.

2. Menville, J. G., and Archinard, J. J.: Skin Eruptions in Patients Receiving Sulfanilamide, J. A. M. A. **109**:1009 (Sept. 25) 1937.

3. Tedder, J. W.: Toxic Manifestations in the Skin Following Sulfanilamide Therapy, Arch. Dermat. & Syph. **39**:217 (Feb.) 1939.

4. Caro, M. R.: Pemphigus: Treatment with Sulfanilamide, Arch. Dermat. & Syph. **37**:196 (Feb.) 1938.

5. See for example Feldman, S.: Pemphigus Treated with Sulfanilamide; Sulfanilamide Eruption, Arch. Dermat. & Syph. **39**:601 (April) 1939, and the discussion following.

When he left the hospital, the patient felt perfectly well. However, he was of necessity exposed to the sunshine that afternoon, although the exposure was not excessive. The next day decided edema developed on the face and hands. The skin over the shoulders became reddened, and a patchy erythematous pruritic eruption rapidly spread over his chest and back until his entire body was covered with cutaneous lesions.

I first observed the patient on July 14. At this time he presented a generalized coalescing morbilliform eruption. His face was edematous. Both hands were diffusely swollen to about twice their normal size. He complained of feeling weak, tired and feverish. His temperature, taken orally, was not elevated. The following day large tense bullae appeared on the dorsum of his right hand and on his right forearm. The surrounding skin was not involved except for the underlying edema. During the following two days about twelve such bullous lesions appeared. On the forearm they coalesced to form a multilocular plaque.

He made a prompt recovery with local therapy and was completely free of lesions on July 21.

COMMENT

It is not claimed that the bullous eruption in this patient could have been confused with that of pemphigus on the basis of the distribution of the lesions or of the course of the eruption. However, the individual bullae on the right hand and forearm were clinically indistinguishable from those seen in pemphigus. Therefore, in treating this disease with sulfanilamide one must realize that apparent clinical progression may be due to a toxic reaction to the drug rather than to the disease itself. Each case must be evaluated in the light of the knowledge that sulfanilamide may cause bullous lesions. Holland [6] noted that the pemphigus in his patient became aggravated when large doses of sulfanilamide were administered.

That this patient was photosensitive is indicated by the initial appearance of the eruption on the exposed portions of the body, i. e. the face and the dorsa of the hands as well as by its maximum intensity in these areas. The fact that the reaction did not start until after exposure to sunlight further confirms this.

Perhaps the solar sensitivity constituted the basic etiologic agent in the production of the bullae. This would be analogous to the blister formation occasionally encountered in pellagra and severe sunburn. However, this patient said that he had not had more than minimum exposure to the sun, and there was no erythema present to lend clinical confirmatory evidence of sunburn.

SUMMARY

A report is presented on a patient in whom a bullous eruption developed after the administration of sulfanilamide.

6. Holland, M., in discussion on Feldman.[5]

It is suggested that the employment of sulfanilamide in the treatment of pemphigus may lead to confusion, as the medication may cause lesions similar to those seen in the disease being treated.

NOTE.—While this paper was in press, two additional examples of bullous eruptions following sulfanilamide therapy have been reported. Bettley and Simon [7] described a similar case. A patient with a severe bullous eruption following the ingestion of sulfapyridine was exhibited by Omens and Robbins [8] before the Chicago Dermatological Society on March 15, 1939.

1624 Franklin Street.

7. Bettley, F. R., and Simon, P.: A Bullous Eruption Due to Sulphanilamide, Brit. M. J. **1**:1177 (June 10) 1939.

8. Omens, D. V., and Robbins, J. B.: Severe Toxic Bullous Eruption Following the Use of Sulfapyridine, Arch. Dermat. & Syph. **40**:633 (Oct.) 1939.

DANGERS IN THE USE OF COSMETICS

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Cole [1] has stated:

> There seems to be an alarming increase in the use of cosmetics—and along with this a coincident increase in the dangers due to their use. The esthetics of cosmetics are the concern of the physician only secondarily; but we should do everything in our power to call to the attention of the public the damage resulting from their use.

To the average person, whether physician or layman, cosmetics represent a highly commercialized development of the current century; their composition and the dangers attendant on their use are known to but a few select groups. Lerner [2] reported that cosmetics have been used by women from the time of the earliest records and quoted numerous recipes for beauty which were in vogue perhaps more than twenty thousand years ago. Oddly enough, a study of various historical references [3] to the nature of cosmetics reveals that the so-called "modern cosmetics" can be traced back many centuries.

Lain [4] stated:

> Cosmetics did not present a serious pathologic problem until after the beginning of the twentieth century. Cases of cosmetic dermatoses became so frequent between the years 1910 to 1925 that public health agencies began an organized attack.

Wilbert,[5] of the United States Public Health Service, in 1915 presented a collection of various reports of injuries from cosmetics.

There have been sporadic organized attempts against the use of dangerous cosmetics, but most of the available references have dealt with small groups or even single cases of injuries from cosmetics. The

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The material in this paper represents work done for the Department of Public Health while the author was a student at the College of Physicians and Surgeons, Columbia University. The review is based on articles published before the establishment of the Food, Drug and Cosmetic Act of 1938, and the descriptions cited do not necessarily represent the composition of the respective cosmetics at the present time.

1. Cole, H. N.: The Dermatoses Due to Cosmetics, J. A. M. A. **82**:1909-1911 (June 14) 1924.

2. Lerner, C.: History of Feminine Beautification, Arch. Dermat. & Syph. **26**:1022-1031 (Dec.) 1932.

3. (*a*) Downing, J. G.: Cosmetics—Past and Present, J. A. M. A. **102**:2088-2091 (June 23) 1934. (*b*) Levin, O. L.: Cosmetics—Use, Historical and Modern, M. Rec. **139**:292-294, 1934. (*c*) Lerner.[2]

4. Lain, E. S.: Cosmetic Eruptions, South. M. J. **25**:718-722, 1932.

5. Wilbert, M. I.: Cosmetics as Drugs, Pub. Health Rep. **30**:3059-3066, 1915.

purposes of the present paper are to present an organized review of selected literature on cosmetics, to indicate briefly the composition of important cosmetics; to report proved cases of damage from their use and to indicate to what extent the consumer is protected by law, by the medical profession and by other agencies. For the reports cited I make no claim to completeness, with respect either to the nature of the cosmetics or to their dangers.

INCIDENCE OF INJURIES FROM COSMETICS

Tobias,[6] in 1932, declared that the list of dermatoses due to external irritants is so large that one is impressed with the importance of having a list of irritants available for reference. In 1933 Hollander [7] reported that dermatitis produced by cosmetics through direct contact was becoming a more frequently established and recognized condition but that the specific agent responsible had to be ferreted out of an almost endless number of so-called beauty preparations. One year later Downing [3a] added his observations that with such a great increase in the cosmetic business there has been an alarming increase in the number of local disturbances of the skin and that some systemic results have been reported; every busy dermatologist observes one or more cases a week of some condition resulting from cosmetics, but few report these cases.

Goodman,[8] an outstanding authority in cosmetic dermatology, reported in 1930 that the number of persons who are sensitive to the ingredients of ordinary cosmetics is small; on the whole, throughout the country, it would be difficult to collect at any one time 100 persons who have been harmed by the application of cosmetics. Goodman, however, admitted that in many cases cosmetic injury is unrecognized by the ordinary practitioner.

In 1927 Cole [9] reported the results of an investigation conducted by the American Medical Association, comprising 62 returns from a questionnaire sent to 437 dermatologists throughout the United States and 23 reports from another source. There were 111 reported cases of injury from hair dye (of which only 74 were reported by dermatologists). Of 137 reports of injury from various cosmetic nostrums, only 43 were reported by dermatologists. Forty-three additional cases of injury from hair tonic were reported, and injuries from the use of twenty-three miscellaneous preparations were listed. There was no indication of the period during which these injuries occurred.

6. Tobias, N.: Cosmetics, J. Missouri M. A. **29**:63-69, 1932.

7. Hollander, L.: Dermatitis Produced by Cosmetics, J. A. M. A. **101**:259-261 (July 22) 1933.

8. Goodman, H.: Cosmetics and Your Skin, Hygeia **8**:123-125 (Feb.) 1930.

9. Cole, H. N.: Investigation of Injuries from Hair Dyes, Dyed Furs and Cosmetics, J. A. M. A. **88**:397-399 (Feb. 5) 1927.

At the Lain-Roland clinic (Oklahoma City) in 1930, there were 285 cases of dermatitis of various types; in 42, or 11 per cent, of such cases, the eruption occurred over the face; a diagnosis of cosmetic dermatitis was made in 32, or 75 per cent, of the series of facial eruptions; this represented about 11 per cent of all cases of dermatitis observed during the year.[4]

It is thus evident, although adequate statistics are lacking, that the incidence of injury from cosmetics is extremely small, especially so when one considers the extent of the cosmetic industry and the tremendous number of persons using these preparations several times each day. Nevertheless, a problem does exist, and the physician and the public health officer should be aware of the fundamental principles involved.

The earlier and more severe cosmetic injuries were to a great extent systemic poisonings from dangerous substances, such as lead and mercury. The cosmetic manufacturers today, cognizant of these earlier, more or less tragic experiments, have rid their industry of substances causing severe systemic reactions; in fact, in fairness to the industry, it should be reported that many of the larger and more reputable firms maintain laboratories for the purpose of eliminating harmful ingredients.

At present, the injuries from cosmetics seem to have been reduced to dermatologic, and more particularly allergic, manifestations. The cosmetic racketeer of today is that one who uses ingredients in his products that simply make a better physical and esthetic preparation, regardless of their nature or their potential dangers, and many racketeering companies exist and flourish at present.

Germany seems to have made considerable progress in regulation of the cosmetic industries. With respect to statistics, Krantz [10] reported that, of some 2,500,000 Germans that regularly dye their hair, 20 of 30,000 are slightly affected by the dye and 400 of 500,000 severely so. "Most of the metallic dyes are forbidden in Germany." The use of lead in cosmetics in Germany has been forbidden for at least forty years, according to Carleton.[11]

TOILET POWDERS—COMPOSITION AND DANGERS

Carleton [11] stated:

> Toilet powders consist of a mixture of animal or vegetable powders, colouring matter, and perfume. The vegetable powders include rice, wheat, corn flour, starch, acacia, and tragacanth. The mineral powders in use are chalk, talc, kaolin, magnesium carbonate, bismuth nitrate or carbonate, and zinc oxide. The dyes may be of vegetable origin or may be aniline derivatives. Various ethereal oils are used as perfumes, and orris root is frequently employed as a fixative.

10. Krantz, W.: Injuries to the Skin Caused by Cosmetics, Med. Klin. **32**: 209-212, 1936.

11. Carleton, A.: Cosmetics: Uses and Dangers, Brit. M. J. **1**:999-1001, 1933.

In addition, some widely advertised powders contain impurities and metals such as lead, bismuth, arsenic and mercury.[3b] The most dangerous powder ingredient, which apparently is scarcely used at present in any part of the cosmetic industry, is lead; lead carbonate and lead acetate produce excellent powders from the physical and esthetic aspect.

That vegetable powders injure the skin through swelling of the granules of powder in the cutaneous fat and that mineral powders irritate because of sharp edges and spicules of grains of some powders, especially those containing calcium sulfuricum and terra silicea, was stated by Kapp.[12]

As early as 1881 there were reports of systemic poisoning from a cosmetic containing lead carbonate; Holland [13] reported the cases of 2 sisters, in whom poisoning was demonstrable by bilateral wrist drop and spasms. In Barron and Habein's [14] famous report of 1921 were described 5 cases (in 4 of which the damage was fatal) of lead poisoning in the women of a single family, resultant from the steady use of a powder, "flake-white," composed of pure lead carbonate.

Tuttle [15] observed 5 cases of poisoning in 1884 from a cosmetic powder containing an insoluble preparation of bismuth.

It is interesting to note the increase in the apparently allergic reactions to certain ingredients of face powders, notably orris. Freudenthal [16] reported several cases of allergic disturbance of the upper part of the respiratory tract, in one of which the condition was proved to be due to orris in face powder.

The results of a study by Balyeat [17] of 1,000 cases of hay fever and asthma are extremely interesting from the point of view of the dangers of using face powders containing orris. Of 180 cases of hay fever and asthma in patients under 14 years of age, in 18, or 10 per cent, there was a reaction to orris. Of 82 cases of perennial hay fever in adults, in 39, or 47.5 per cent, there was a definite reaction to orris. Of 365 cases of asthma studied, orris was the sole cause in only 1, a chief factor in 26, or 7.1 per cent, and a contributing factor in 48, or 10.4 per cent. Of 373 cases of seasonal hay fever, there was a reaction to orris in 27, or 7.2 per cent, in spite of the etiologic importance of pollen

12. Kapp, cited by Downing.[3a]

13. Holland, J. W.: Chronic Lead Poisoning from Lead Cosmetics, Rep. Bd. Health, Kentucky (1880) **3**:lvii-lxi, 1881.

14. Barron, M., and Habein, H. C.: Lead Poisoning, with Special Reference to Poisoning from Lead Cosmetics, Am. J. M. Sc. **162**:833-862, 1921.

15. Tuttle, cited by Cole.[1]

16. Freudenthal, W.: Tobacco, Alcohol and Cosmetics in Relation to Upper Respiratory Tract, Laryngoscope **37**:217-230, 1927.

17. Balyeat, R. M.: The Importance of Orris Root as an Etiologic Factor in Hay Fever and Asthma, J. Lab. & Clin. Med. **13**:516-522, 1928.

in seasonal disease. Cooke,[18] Phillips [19] and Rackeman [20] reported similar results of determinations of hypersensitivity to orris among patients with hay fever and asthma, although their figures were somewhat lower.

Robinson [21] in 1915 reported 2 cases of lead intoxication, in each of which there were wrist drop, muscular atrophy, a lead line on the gums and paralysis from a lead carbonate face powder.

FACIAL CREAMS—COMPOSITION AND DANGERS

Cold creams, according to Downing,[3a] are prepared from a vegetable or mineral oil, such as oil of almond, yellow wax or liquid petrolatum, to which is added a small amount of sodium borate to aid emulsification. Among other substances which may or may not be present in cold creams are palmitates, stearates and fatty alcohols; lead and mercury are rarely used in these preparations at present. Most of the substances used are relatively innocuous.

Cleansing creams, in spite of the allegation that they replace soap and water, are nothing more than mixtures of liquid petrolatum and higher melting point greases, fats and waxes.

MacKenna's [22] report, written in 1930, indicated that he was almost radically convinced of the dangers of facial creams; he suggested that the paraffin in many cold creams may lead to an increase in the number of cases of rodent ulcer and of epithelioma of the face in women; furthermore, he expressed a belief that the physical action of both cold and vanishing cream leads eventually to the production of acne rosacea. Because of the lack of supportive evidence, one is not inclined to consider MacKenna's fears seriously.

Two experimental investigations of facial creams were apparently inspired by MacKenna's statements. Downing [3a] cited one series in which not a single case of dermatitis occurred from the use of vanishing or cold cream of a special formula in a group of 25 subjects. In another group [11] vanishing cream was used on 40 subjects and proved harmless to 24 (although 3 had naturally dry skins); it proved beneficial in 13 cases, and in only 1 did it cause dryness.

The questionnaire of the American Medical Association, as reported by Cole,[9] showed that of the 137 reports of injury from various cosmetics, 9 were from cold creams, 4 from bleaches, 5 from powders and

18. Cooke, cited by Balyeat.[17]

19. Phillips, cited by Balyeat.[17]

20. Rackeman, cited by Balyeat.[17]

21. Robinson, cited by Cole.[1]

22. MacKenna, R. M. B.: Modern Cosmetic Preparations: Chemical Composition and Pathological Developments Attributable to Them, Brit. M. J. **1**:899-902, 1930.

8 from rouge and the like; mercury bichloride and ammoniated mercury were found to be the commonest offending ingredients.

Woltman [23] described in 1922 a case of severe systemic lead poisoning in a woman who had used a face cream with a high lead content. As recently as 1936,[24] a case of chronic lead poisoning from a grease paint, of high lead content, was reported. Apparently, then, the manufacturers have failed to profit by the earlier tragic lessons of lead in cosmetics, or they simply choose to ignore the dangers.

Two cases of dermatitis of the eyelids from facial cream, in 1 of which camphor was the offending ingredient and in the other perfume (methylheptine carbonate), were reported by Rattner.[25] In another case [26] atopic dermatitis and angioneurotic edema of the face were reported as due to methylheptine carbonate, the perfume in a facial preparation. These cases occurred rather recently.

In 1937 a dermatologist queried the Bureau of Investigation of the American Medical Association as to the ingredients of Jergen's lotion, as he had a patient with a severe dermatitis from its use (patch test positive). Because of the failure of the manufacturer to cooperate, it was impossible to trace the offending ingredient.[27]

LIPSTICKS—COMPOSITION AND DANGERS

Sulzberger and Goodman [28] said:

> The lipstick in common use has a fatty base, commonly containing several of the following ingredients: yellow wax, paraffin, petrolatum, hydrous wool fat, castor oil, stearic acid and cetyl alcohol. . . . In this base are incorporated perfumes, dyes and lakes.

According to Baer,[29] a dibrom or tetrabrom derivative of fluorescein is used to set the color and make it permanent; the dyes used in the manufacture of lipstick are of vegetable and aniline origin.

Sulzberger and Goodman [28] reported a series of recent cases, 12 of cheilitis and 2 of dermatitis of the face (without cheilitis), due to lipstick; 8 of the patients were hypersensitive to the indelible dyes

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23. Woltman, H. W.: Lead Poisoning from Face Enamel, J. A. M. A. **79:** 1685 (Nov. 11) 1922.

24. Bartleman, E. L., and Dukes, C.: Chronic Lead-Poisoning Due to Theatrical Grease Paint, Brit. M. J. **1:**528-530, 1936.

25. Rattner, H.: Dermatitis of Eyelids, J. A. M. A. **103:**180-181 (July 21) 1934.

26. Hoffman, M. J., and Peters, J.: Dermatitis Due to Facial Cream, Caused by Methyl Heptine Carbonate, J. A. M. A. **104:**1072 (March 30) 1935.

27. Jergen's Lotion: A Lesson in the Art of Correspondence, report of the Bureau of Investigation, J. A. M. A. **108:**135-136 (Jan. 9) 1937.

28. Sulzberger, M. B., and Goodman, J.: Acquired Specific Hypersensitivity to Simple Chemicals: II. Cheilitis, with Special Reference to Sensitivity to Lipstick, Arch. Dermat. & Syph. **37:**597 (April) 1938.

29. Baer, H. L.: Lipstick Dermatitis, Arch. Dermat. & Syph. **32:**726-734 (Nov.) 1935.

(bromfluorescein derivatives) and 7 to a certain azo dye in the lipsticks; there was no sensitivity to methylheptine carbonate (perfume) in any case; in all cases benefit was obtained by the substitution of another lipstick of special formula. These same authors concluded that cheilitis due to lipstick is relatively rare and usually due to hypersensitivity to one or more of the dyes and pigments of the lipstick.

Sulzberger and Goodman cited from the French literature cases of marked eczematous hypersensitivity to hydrous wool fat.

In an important and extensive article, Baer [29] reported a case of lipstick dermatitis; with the aid of the manufacturer, he was able to test each of the ingredients, and methylheptine carbonate (a synthetic perfume derived from castor oil) was proved to be the offending agent. Baer conducted further studies of the perfume ingredient and found that of 38 women who used lipstick (without reaction) 50 per cent were sensitive to methylheptine carbonate and, further, that of 10 men, who did not use liptick, 4 showed irritation from the perfume. Methylheptine carbonate is currently a widely used synthetic perfume.

Freudenthal [16] reported a case of severe allergic disturbance of the upper part of the respiratory tract from the use of lip rouge.

NAIL POLISHES—COMPOSITION AND DANGERS

"Nail lacquers are solutions of nitrocellulose in various solvents, with the addition of certain aids to solution and plasticizers to make the film flexible."[30] Typical solvents are acetone, butyl acetate and amyl acetate; typical aids to solution, toluene, benzene, xylene and naphtha, and typical plasticizers, castor oil, camphor and rosin.

These preparations for the nails are apparently the least harmful of all the cosmetics, although minor disturbances of the nails are frequent. In general, the nails become brittle, and there is a splitting, characterized chiefly by the uplifting of scales of unequal keratin, principally at the tips of the nails. Acetic acid has been alleged, by certain authors, to be liberated from the lacquers and to cause the irritation; [30] it has also been stated that the injuries are due to the drying action of the solvents.

In an investigation of 25 cases (all in business women using the same brand of nail enamel), I found that nearly half of the group showed brittleness and splitting of the nails in some degree; strangely enough, the other half of the group were able to wear the polish without any sign of irritation.

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30. Nail Polishes and Lacquers, Queries and Minor Notes, J. A. M. A. **110**: 1943-1944 (June 4) 1938.

One case of leukoplakia due to nail enamel has been reported.[31] In another case of nail polish dermatitis, ethylene dichloride (the solvent) was found responsible.[32]

Hollander [7] declared that nail paints and manicuring aids produce a scaling of the nail plates and occasionally an inflammation of the nail bed. On the other hand, Downing [3a] expressed the belief that liquid nail polishes may be of value by their antispectic qualities in the prevention of infections that might have resulted from the none too sterile operating tools of the manicurist.

HAIR DYES—COMPOSITION AND DANGERS

According to Carleton,[11] hair dyes include (1) vegetable dyes, such as henna; (2) metallic dyes, such as silver, copper, mercury, lead, nickel, cobalt and bismuth, in which the metal combines with the sulfur in the hair to form a deposit of metallic sulfide; (3) compounds of metallic salts and vegetable products, such as pyrogallic acid, and (4) aniline derivatives, of which the best known is paraphenylenediamine.

Of all the cosmetics, the hair dyes are the worst offenders. Not only are simple irritations reported throughout the literature from the use of hair dyes, but the most severe of systemic poisonings are reported and in an unusually large number of cases. The story of poisoning by hair dye is not a new one.

Many cases were reported in the latter part of the nineteenth century and throughout the early part of the current century. Berger [33] in 1909 reported a case of temporary impairment of vision in a woman who had used a paraphenylenediamine-containing dye; the author cited several French authors to the effect that many severe cases of aniline dye poisoning from the use of hair dyes were being reported in the French literature.

Three cases of dermatitis due to hair dyes containing paraphenylenediamine were reported by Knowles [34] in 1916. The author dealt with general considerations on the topic extensively.

In the 111 cases of injury due to hair dye reported in the answers to the questionnaire cited previously [9] such dangerous ingredients as lead acetate, sulfur and pyrogallol were found in the dyes; paraphenylenediamine was present in nineteen of the forty-one dyes tested.

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31. Greenbaum, S. S.: Leukoplakia of Unusual Origin (Nail Enamel), Arch. Dermat. & Syph. **33**:538 (March) 1936.

32. Goodman, J., and Sulzberger, M. B.: Acquired Specific Hypersensitivity to Simple Chemicals: I. Eczematous Sensitivity to Clothing and to Cosmetics, with Special Reference to Dyes, J. Allergy **9**:136-152, 1938.

33. Berger, E.: Visual Disturbance Due to the Use of Hair Dye Containing Aniline, Arch. Ophth. **38**:397-400, 1909.

34. Knowles, F. C.: Dermatitis Caused by Cosmetics and Wearing Apparel, Particularly Those Containing Paraphenylendiamine, Pennsylvania M. J. **19**:897-900, 1916.

Miller and Taussig [35] reported 2 cases of severe dermatitis from the use of preparations containing aniline; in 1 case permanent baldness resulted six months later. In 3 cases from the British literature [36] severe systemic reactions were reported to be due to aniline hair dyes. A fourth report from the British literature [37] described a peculiar case of fatal asthma from the use of a hair preparation in a 40 year old man.

The consensus is that the reactions from aniline dyes are based on a hypersensitivity, which all persons have in some degree, to dyes containing paraphenylenediamine.

Hair tonics have been mentioned occasionally as a source of irritation; the offending ingredients are chiefly quinine, salicylic acid and resorcinol. Cole [1] reported 3 cases of severe reaction from the use of tonic; the offending ingredients were, respectively, lead, arsenic and salicylic acid. Gelfand [38] reported another case of dermatitis due to arsenic in a hair tonic.

Among cases of irritation due to preparations for the hair, dermatitis has been reported in 1 case [39] as due to quinine in a dandruff cream; in 1 case [40] perennial hay fever was attributed to lycopodium in a powder for oily scalp, and in another case [41] an eruption was regarded as due to a shampoo.

Wave-setting preparations are mucilaginous substances which are used for producing or setting "natural" waves of the hair. Most of them consist of a mucilaginous gum, water and perfume; in several cases a reaction to such preparations has been reported in the literature. Hollander [7] reported 3 cases of dermatitis due to a proprietary preparation (la gerardine), the offending ingredient of which could not be determined. A case of perennial hay fever has been reported [42] as due to the karaya gum in a wave-setting fluid. Feinberg [43] reported an analogous case, in which persistent asthma was due to the karaya gum in a wave-setting fluid.

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35. Miller, H. E., and Taussig, L. R.: Cosmetics, J. A. M. A. **84**:1999-2002 (June 27) 1925.

36. Injury from Hair Dye, Medical News, Brit. M. J. **1**:373, 1922. Injury from Hair Dye, Medicine and the Law, Lancet **1**:1058, 1926. Nott, H. W.: Systemic Poisoning by Hair Dye, Brit. M. J. **1**: 421-422, 1921.

37. Oliver, T.: Saturnine Asthma, Lancet **2**:907-909, 1922.

38. Gelfand, H. H.: Hypersensitiveness to Arsenic: Dermatitis from Liquid Arvon (Hair Tonic), J. Allergy **7**:254-260, 1936.

39. Johnson, D. W.: Dermatitis Due to Application of Dandruff Cream, Urol. & Cutan. Rev. **39**:173, 1935.

40. Lambright, G. L., and Albaugh, R. P.: Perennial Hay Fever from Lycopodium: Report of a Case, J. Allergy **5**:590-591, 1934.

41. Balyeat, R. M.: Cosmetic Dermatitis, Northwest Med. **34**:12, 1935.

42. Bullen, S. S.: Perennial Hay Fever from Indian Gum (Karaya Gum), J. Allergy **5**:484-487, 1934.

43. Feinberg, S. M.: Karaya Gum Asthma, J. A. M. A. **105**:505 (Aug. 17) 1935.

EYELASH DYES—COMPOSITION AND DANGERS

Darkening of the eyebrows and eyelashes is accomplished in two ways, according to Greenbaum:[44] (1) by coating the hairs (with mascara or lamp black) and (2) by actually staining them (usually with a regular hair dye).

The "mild epidemic" of tragic reactions from the use of a proprietary preparation (lash-lure) early in the present decade is well known and has been widely reported in the literature.

Bilateral necrosis of the cornea resulting from the use of lash-lure and leaving the user light perception only was reported by Moran.[45] The same result occurred in a case reported by McCally, Farmer and Loomis.[46] Three cases in which there was no serious impairment of vision have been described.[47]

One case in which the termination was fatal was described by Forbes and Blake.[48] These authors were tremendously impressed with the severe systemic reaction to the paraphenylenediamine contained within lash-lure. There was a possibility in this case that sepsis was the cause of death, the portal of entry being the ophthalmic lesions.

PERFUMES—COMPOSITION AND DANGERS

Perfumes are of complex composition. Baer[29] stated.

> Animal perfumes, balsams and natural perfumes were utilized before the development of synthetic perfumes; these last are principally the esters, ketones and aldehydes of the coal tar products.

Since the advent of synthetic perfumes there have occurred a large number of reactions to perfumes and to perfumed products. Essentially, these reactions are characterized by a curious photopigmentation, described by many authors as "berlock dermatitis."

Two cases were reported by Goeckermann[49] in 1922. In 1930, 5 additional cases were described by Gross and Robinson.[50]

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44. Greenbaum, S. S.: Dermato-Conjunctivitis Due to Lash-Lure, an Eyelash and Eyebrow Dye, J. A. M. A. **101**:363-364 (July 29) 1933.

45. Moran, C. T.: Bilateral Necrosis of Cornea Following Use of Hair Dye on Eyebrows and Eyelashes, J. A. M. A. **102**:286-287 (Jan. 27) 1934.

46. McCally, A. W.; Farmer, A. G., and Loomis, E. C.: Corneal Ulceration Following the Use of Lash-Lure, J. A. M. A. **101**:1560-1561 (Nov. 11) 1933.

47. Bourbon, O.: Severe Eye Symptoms Due to Dyeing the Eyelashes, J. A. M. A. **101**:1559-1560 (Nov. 11) 1933. Harner, C. E.: Dermato-Ophthalmitis Due to the Eyelash Dye Lash-Lure, ibid. **101**:1558-1559 (Nov. 11) 1933. Jamieson, R. C.: Eyelash Dye (Lash-Lure) Dermatitis with Conjunctivitis, ibid. **101**:1560 (Nov. 11) 1933.

48. Forbes, S. B., and Blake, W. C.: Fatality Resulting from Use of Lash-Lure on Eyebrows and Eyelashes, J. A. M. A. **103**:1441-1442 (Nov. 10) 1934.

49. Goeckermann, W. H.: A Peculiar Discoloration of the Skin, J. A. M. A. **79**:605-607 (Aug. 19) 1922.

50. Gross, P., and Robinson, L. B.: Berlock Dermatitis, Arch. Dermat. & Syph. **21**:637-641 (April) 1930.

In an interesting article in 1930 Lane and Strauss [51] presented an extensive review of the subject and produced considerable evidence to point toward oil of bergamot as the offending ingredient and cause of this peculiar photopigmentation.

Goodman [52] described another case in 1931 and declared that "perfume dermatitis is probably more common than the rarity of its appearance in medical literature would indicate." Seven other cases in which oil of bergamot was considered the offending substance have been described by various authors.[53]

DEPILATORIES—COMPOSITION AND DANGERS

Carleton [11] stated:

> Barium sulphide is the commonest constituent of most depilatories, but sulphides of calcium, strontium, sodium or magnesium are also used; these appear to be generally harmless, but in sensitive skins, they may give rise to a generalized dermatitis.

Thallium acetate was used in the past, but because of its intensely toxic action, it has more or less been discarded.

Hollander [7] expressed the belief that depilatories produce an indolent folliculitis which sooner or later becomes suppurative and then spreads by contiguity.

"Koremlu" is a famous proprietary depilatory which rode to fame not on its beneficial effects but on the widespread destruction it caused its users. Winters [54] declared in 1936:

> This product contained 7 per cent thallium acetate, a deadly poison commonly used to kill rats. Baldness, skin injury, nervous and glandular troubles were some of the effects produced by Koremlu.

VITAMINS IN COSMETICS

In the past few years a new phase has appeared in the development of cosmetics, namely, the introduction of preparations containing vitamins. These are alleged to benefit the skin in various ways, from correcting "subnormal conditions of the skin" to "smoothing out the wrinkles and lines of old age."

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51. Lane, J. E., and Strauss, M. J.: Toilet-Water Dermatitis with Especial Reference to "Berlock" Dermatitis, J. A. M. A. **95**:717-719 (Sept. 6) 1930.

52. Goodman, H.: Perfume Dermatitis, Brit. J. Dermat. **43**:177-184, 1931.

53. Downing, J. G.: Pigmentation from Perfume: Berlock Dermatitis, New England J. Med. **207**:660-662, 1932. Greenbaum, S. S.: Cutaneous Photo-Pigmentation and Cosmetics, with Special Reference to Berlock Dermatitis, Pennsylvania M. J. **38**:28-31, 1934. Tobias, N.: Emeraude Perfume Dermatitis, J. A. M. A. **104**:1322-1323 (April 13) 1935.

54. Winters, S. R.: Public Enemies No. 1: Food, Drug and Cosmetic Racketeers, Hygeia **14**:832-835 (Sept.) 1936.

The use of vitamins in cosmetics will probably cause little if any harm; moreover, their efficacy will parallel their harmfulness. In 1937 *The Journal of the American Medical Association* discussed editorially [55] the complaint of the Federal Trade Commission against the manufacturer of a toilet soap containing vitamin D. Although the complaint was essentially against the fraudulent claims of the manufacturer, question was raised in the editorial whether vitamins exert any beneficial effect on the skin, even assuming the ability of the skin to absorb such substances.

PROTECTION OF THE COSMETIC CONSUMER

Fortunately for the consumer, the majority of cosmetics are relatively harmless. Most of these articles are useless as well. It is the protection of the consumer not from fraudulent and misbranded claims but from exposure to cosmetics which contain ingredients potentially dangerous to health with which this paper is concerned.

Aside from a few items of local legislation, principally against selected dangerous products, there were no restraints, federal, state or local, against the manufacture, sale or use of any cosmetic preparation until passage of the Federal Food, Drug and Cosmetic Act of 1938.

Intended to replace the Federal Food and Drug Act of 1906 (an act which failed to define cosmetics or include legislation against them), the new law was approved by the President on June 25, 1938, but it did not become wholly effective until June 25, 1939, in order to allow the various industries concerned time to conform with the provisions of the new act.

A report of the Bureau of Legal Medicine and Legislation of the American Medical Association [55a] discloses most of the important provisions of the new act.

Cosmetics are defined by the new act as articles other than soap "intended to be rubbed, poured, sprinkled, or sprayed on, introduced into, or otherwise applied to the human body or any part thereof for cleansing, beautifying, promoting attractiveness, or altering the appearance." Soaps that are represented as being of service in the cure, mitigation, treatment or prevention of disease come, however, within those provisions of the new act that relate to drugs.

Poisonous or deleterious ingredients are forbidden, but only when it can be shown that they may render the cosmetic injurious to the user under the conditions of use prescribed in the labeling or under such conditions as are customary or usual.

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55. No Sunshine in Soap, editorial, J. A. M. A. **109**:509-510 (Aug. 14) 1937.

55a. The New Federal Food and Drug Act at Last, editorial, J. A. M. A. **111**:324-326 (July 23) 1938.

Coal tar hair dyes are expressly permitted, except dyes for eyelashes or eyebrows, if cautionary statements are printed on the label. No ingredient of any kind need be disclosed on the label.

Any toilet article represented as having the power of preventing, mitigating or curing disease is, however, a "drug" within the meaning of the law and is subject to regulation as a drug.

Because of the broad provisions of the act as it pertains to cosmetics, its ability to protect the cosmetic consumer is doubtful and can be estimated only by actual trial. The outlawing of coal tar eyelash and eyebrow dyes is an excellent provision. The ruling against poisonous and deleterious ingredients, although vague, should help to reduce the incidence of injuries due to cosmetics.

It is somewhat unfortunate that the law does not require listing of ingredients on the label, because in this manner potentially dangerous substances would be known to the consumer and, secondarily, racketeering prices for ingredients of low actual cost would be reduced.

It should be remembered that the new law regulates cosmetics only in interstate and foreign commerce, which for the purposes of the law includes commerce within the District of Columbia and certain other exclusively federal jurisdictions. The cosmetic racketeer will still flourish in intrastate commerce unless the states themselves adopt the provisions of the Federal act or others at least equally effective.

The American Medical Association has accomplished much for the protection of the consumer, first, in investigating cases of actual injury from cosmetics and, second, in exposing fraudulent claims. The Bureau of Investigation of the American Medical Association publishes a pamphlet [56] devoted chiefly to the exposure of unscientific products.

It would seem moderately important, therefore, that the average physician and public health officer be aware of the nature and the potential dangers of the use of cosmetics; he may be consulted concerning injury from a cosmetic or asked the efficacy of some particular device. After reviewing the subject, I am amazed at the number and the variety of substances that persons expose themselves to in using the many cosmetic preparations.

Goodman,[57] in 1935, cited a case of dermatitis from a combination of two cosmetics, neither of which alone caused a reaction. It is surprising that more such occurrences have not been reported.

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56. Cosmetics and Allied Preparations, Bureau of Investigation, Chicago, American Medical Association, 1937.

57. Goodman, H.: Skin Reactions to Combinations of Two Toilet Articles Neither of Which Alone Caused Irritation, Arch. Dermat. & Syph. **32**:632 (Oct.) 1935.

SUMMARY

Selected literature on the composition of and dangers in the use of important cosmetics (toilet powders, facial creams, lipsticks, nail polishes, hair and eyelash dyes, perfumes and depilatories) is reviewed briefly.

Adequate statistics are lacking, but the incidence of severe injury from the use of cosmetics is relatively low in comparison with the number and the variety of cosmetics used.

Earlier cosmetics frequently resulted in severe systemic poisonings (from lead, mercury, etc.), but the majority of injuries from cosmetics at the present time belong in the field of allergic dermatoses.

The aniline dyes and coal tar derivatives, in particular the paraphenylenediamine group, are the most serious offenders. Hair dyes, especially preparations for the eyelashes, are extremely dangerous. I wonder how any person can put an unknown, foreign substance in close approximation to such an important structure as the eye.

A new field of cosmetic manufacture, that of synthetic perfumes, is giving rise to many dermatoses. Nail polishes, although relatively innocuous, may cause extensive physical disturbance of the nails.

Reference is made to the Federal Food, Drug and Cosmetic Act of 1938, designed to regulate interstate and foreign commerce in these items. The new law defines cosmetics, outlaws ingredients proved to be deleterious or poisonous and rules against coal tar eyelash and eyebrow dyes. Other coal tar dyes are permitted. No cosmetic ingredient of any kind need be listed on the label.

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LXXXVI.—AN INQUIRY INTO THE CAUSE OF PEMPHIGUS

IS IT A VIRUS DISEASE?

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ST. LOUIS

Chronic pemphigus vulgaris is a name used to identify a definite disease. Since the principal symptom and primary lesion of this disease is the appearance on the skin and mucous membranes of a number of uncomplicated blisters and since somewhat similar lesions may occur in other diseases, the diagnosis of pemphigus is often a confusing problem in certain cases. There are borderline cases in which dermatitis herpetiformis, erythema multiforme, lupus erythematosus and even certain general infections of the blood stream may be accompanied by numerous bullae and may run a course simulating pemphigus to such a degree that in the absence of other than clinical criteria differentiation is almost a matter of personal opinion or even guesswork. Such cases are relatively rare, but there is a sufficient number of them in the experience of most dermatologists to color the general concept of just what pemphigus is and where it should be placed in the classification of diseases. In a recent European symposium on pemphigus, the chronic vulgaris type was generally identified as a separate and distinct disease.[1]

In the last few years knowledge of filtrable viruses in general has been increasing, and new methods of demonstrating viruses have been devised. Certain diseases previously of unknown cause have been shown to be due to filtrable viruses. For these reasons, one of us (F. S. M.) has been devoting his time to a study of a number of cutaneous diseases of unknown origin in an attempt to find and demon-

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Studies, observations and reports from the Dermatological and Research Departments of the Barnard Free Skin and Cancer Hospital, service of Dr. M. F. Engman Sr.

1. Du Bois, C.: Comment se faire une opinion sur le problème des pemphigus d'après l'observation clinique, Schweiz. med. Wchnschr. **68**:777, 1938; abstracted, Wise, F., and Sulzberger, M. B.: Year Book of Dermatology and Syphilology, Chicago, The Year Book Publishers, Inc., 1938, p. 167.

strate filtrable viruses. In the course of this work, special effort was devoted to a study of pemphigus vulgaris. Seven typical cases were investigated.

The method chosen in the present investigation has been the technic of chick embryo inoculation as developed by Goodpasture [2] and his colleagues for the study of filtrable viruses and other infectious agents. The chick embryo with its enveloping membranes offers three outstanding advantages as an experimental medium. First, perhaps because of their high metabolic and growth rates, embryonic tissues have a marked degree of susceptibility to virus infection. To date, some twenty-five or thirty viruses have been cultivated in the developing chick, and to the majority of these infectious agents the adult chicken is completely resistant. Thus, to a considerable degree it is possible by the use of embryonic tissues to overcome the experimental difficulties imposed by the more or less specific host requirements of many parasitic micro-organisms. Second, embryonic tissues are for the most part sterile. Certainly they are free from the great variety of parasites which compose the normal flora of the body surfaces and cavities of the adult animal. Because of this sterility, one has a reasonable degree of assurance that the infectious agents isolated from inoculated embryos were those experimentally introduced and not some already resident in the tissues at the time of injection. Finally, from the dermatologic point of view, there is the advantage of having in the chorioallantoic membrane a readily available ectodermal tissue for experimental inoculation. In addition to working with the developing egg, we have employed, with or without modification, some of the methods used by other investigators in the study of pemphigus in experimental animals.

REPORT OF CASES

CASE 1.—R. K., a white woman 76 years of age, was observed and treated in the Barnard Free Skin and Cancer Hospital for about ten months. Over the entire body and in the mouth there was a diffuse bullous eruption typical of pemphigus vulgaris. The results of laboratory and other examinations were not remarkable. The patient recovered after prolonged treatment with injections of iron cacodylate and with blood transfusions. She has remained well for a year.

CASE 2.—M. B., a white woman 49 years of age, entered Barnard Hospital March 22, 1938, suffering from typical pemphigus vulgaris of eleven months' duration. The results of laboratory and other examinations were not remarkable. The patient died of terminal bronchopneumonia June 25, 1938.

CASE 3.—M. K., a white woman 28 years of age, was admitted to the Jewish Hospital May 24, 1938, suffering from a severe bullous eruption over the body and in the mouth. She did not improve with any treatment and died Oct. 18, 1938. Since in addition to the bullae over the body there was also foul-smelling vegetation in the axillas, a diagnosis of pemphigus vegetans was made. She died of pemphigus.

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2. Goodpasture, E. W.: Some Uses of Chick Embryo for the Study of Infection and Immunity, Am. J. Hyg. **28**:111, 1938.

CASE 4.—G. S., a white man 65 years of age, was admitted to the Jewish Hospital on June 1, 1938, suffering from generalized severe bullous eruption of six months' duration. A diagnosis of pemphigus vulgaris was made. The patient remained in the hospital under observation and treatment for about three months. His treatment consisted mainly of injections of iron cacodylate. At the time of his discharge he was improved.

CASE 5.—A. N., a white woman 28 years of age, was admitted to the Jewish Hospital on Oct. 16, 1938, and remained only four days. She had a generalized bullous eruption of three months' duration. A diagnosis of pemphigus was concurred in by most of the dermatologists who examined this patient. However, there was some difference of opinion, and the possibility of bullous erythema multiforme was not ruled out in the opinion of some observers.

CASE 6.—E. M., a white woman 60 years of age, had a vesiculobullous eruption which began six months before she entered the Barnard Free Skin and Cancer Hospital. At the time of entry the patient was suffering from a well developed profuse bullous eruption typical of pemphigus vulgaris. The results of laboratory and other examinations were not remarkable. The phytopharmacologic index was 66 per cent in October 1938 and 43 per cent in January 1939.

CASE 7.—B. Y., a white woman 46 years of age, entered Barnard Hospital in January 1939, suffering from generalized pemphigus vulgaris of one year's duration. She remained in the hospital under observation and treatment for two months and then left under protest. The results of laboratory and other examinations were not remarkable.

REPORT OF EXPERIMENTS

EXPERIMENT 1.—Eggs incubated for nine to twelve days at 38 C. in a commercial incubator were opened by removing a small square of the shell and shell membrane. Onto the exposed chorioallantois, from 0.2 to 0.3 cc. of inoculum was dropped from a 1 cc. tuberculin syringe. The shell opening was closed by ringing it with a sterile mixture of petrolatum and paraffin and placing over it a sterile cover glass. The inoculated eggs were then placed in a bacteriologic incubator and held at 35 C. for four to ten days. The eggs were examined from time to time for evidence of infection.

From three to six eggs were inoculated with blister fluids, either unfiltered or as Berkefeld V filtrates, from all 7 patients with pemphigus, which were removed as soon as possible onto the chorioallantoic membrane of the developing egg. Similarly, from three to six control eggs were inoculated with blister fluid heated to 60 C. for thirty minutes. As a result, although some of the specimens were carried through several passages on the chorioallantoic membrane, none of the fluids from any of the 7 patients gave rise to lesions or changes in the membrane which differed in any way from those observed in the control eggs. Normal chicks hatched from eggs which were allowed complete development.

EXPERIMENT 2.—In order to overcome the possible inhibiting effect of antibodies contained in the blister fluid, decimal dilutions to 1:100,000 were prepared by the addition of physiologic solution of sodium chloride to the blister fluid. Two eggs were inoculated with each dilution. The results were the same as those obtained with undiluted blister fluid.

EXPERIMENT 3.—From 1 patient (case 1), 0.5 cc. of unfiltered blister fluid was injected intracerebrally into each of 2 rabbits, and approximately 0.25 cc. was instilled into the conjunctival sac after scarification of the cornea with a sharp needle; 0.03 cc. of the fluid was injected intracerebrally into each of 6

white mice (Buffalo strain). The same fluid in the form of a Berkefeld V filtrate was similarly injected into 2 rabbits and 6 mice. Seven weeks after inoculation snuffles developed in 1 of the rabbits inoculated with the unfiltered blister fluid, and it died. No lesions were found on gross or microscopic examination of its brain. One of the mice inoculated with the same specimen died five days after the injection. A large abscess in the liver was noted post mortem, but on microscopic examination the brain and kidneys were observed to be free of lesions. No vesicles or ulcerations appeared on the scarified corneas of the rabbits, and all the remaining animals continued symptomless during an observation period of four months.

EXPERIMENT 4.—Twenty-six young white mice were placed in a pasteboard box which was approximately 3 cm. deep and provided with a cellulose acetate window in the lid. The mice were exposed to 400 r of roentgen irradiation. Immediately, each of 3 males and 4 females was inoculated intracerebrally with 0.03 cc. of unfiltered blister fluid from a patient (case 6). Three males and 4 females were similarly inoculated with unfiltered fluid from a patient (case 7). The remaining 4 males and 8 females were intracerebrally inoculated with the combined blister fluids from the 2 patients after the mixture had been heated to 60 C. for a period of thirty minutes. One of the males inoculated with unheated blister fluid from a patient (case 7) was found dead of wounds on the eighth day. A second badly wounded male was etherized, and the brains of both were prepared for histologic examination. Neither brain showed any evidence of meningitis or encephalitis. All of the controls and the remaining test animals of both groups were vigorous and without symptoms at the end of eight weeks' observation.

EXPERIMENT 5.—Blister fluid and blood serum from 2 patients (cases 1 and 2) were injected in amounts varying from 0.1 to 0.5 cc. in separate sites into the shaven skin of rabbits. As a result, a slight inflammatory response occurred at the points of injection, but the reaction rapidly faded, and no bullae or other cutaneous vesicles appeared on the skin of either rabbit.

EXPERIMENT 6.—Bacteriologically sterile blister fluid from 1 patient (case 2) was set up in 1 cc. amounts in plasma clot cultures of minced 8 day old chick tissue. One cubic centimeter of a 25 per cent concentration of normal rabbit serum was added to each culture. Control cultures were similarly set up with normal rabbit serum in place of the pemphigus blister fluid. As a result, although the cultures were periodically examined for several days, no appreciable differences in the rate, amount or character of the growth of the tissues in the two sets of cultures could be observed. Examination of fixed and stained sections of the cultures revealed nothing of significance.

COMMENT

It is our present opinion that pemphigus vulgaris is not caused by a filtrable virus. There is a considerable weight of evidence which points to this conclusion.

Contagion.—In virus diseases characterized by the formation of vesicles, pustules or bullae—such as herpes simplex, varicella, variola, foot and mouth disease or vesicular stomatitis—the virus is abundantly present in the vesicles. If pemphigus were a virus disease, it would seem likely that the fluid from the bullae would contain an abundance

of living virus and that, since special precautions are seldom observed in handling patients with pemphigus, susceptible persons would be exposed to the virus and would acquire the disease. So far as we are aware, however, there is no report of any doctor, nurse or other person so exposed ever acquiring pemphigus vulgaris from a patient.

Experimental Work.—The various attempts reported in this paper to demonstrate a virus pemphigus gave negative results. It might be mentioned, in view of these negative results, that there are virus diseases in which such a high degree of host specificity exists that no experimental animal can be successfully used to demonstrate the virus other than the natural host. Therefore, the negative results of these experiments do not actually rule out the possibility of a pemphigus virus. However, they add to the sum total of evidence against the hypothesis that pemphigus is a virus disease.

Following the report of Urbach and Reiss,[3] there have appeared in the recent literature numerous papers dealing with the virus etiology of pemphigus. Some of the evidence presented in these publications confirms the work of Urbach and his collaborators, and about an equal amount fails to do so. On analysis of the evidence so far presented, it is our opinion that sufficient proof has not been offered to establish a virus as the cause of pemphigus.

While there is still much to be learned about the nature and properties of filtrable viruses, knowledge of them at present is considerable. Because a disease is of unknown causation, that disease is not ipso facto a virus disease. Koch's postulates are as valid for virus infections as for those caused by bacteria. There are few broad generalizations that can be made about filtrable viruses, for they are as diverse in their characteristics as are protozoa, bacteria and fungi. They vary greatly in their range of hosts, in the nature of the lesions which they excite, in the manner of their transmission and in the degree and duration of the immunity which they confer.

In the laboratory, viruses cannot be cultivated in the sterile environment of artificial mediums. This fact requires that viruses be passed from animal to animal, a necessity that is fraught with a certain degree of risk, for laboratory animals as well as man have their quota of viruses and other parasites. It is therefore essential that research on viruses be undertaken with a full knowledge of the spontaneous infections likely to be encountered in experimental animals. Histologic examination of tissues with careful attention to cytologic detail and

3. Urbach, E., and Reiss, F.: Tierexperimentelle Untersuchungen zur Frage der infectiöstoxischen Genese des Pemphigus vulgaris und der Dermatitis herpetiformis Duhring, Arch. f. Dermat. u. Syph. **162**:713, 1930.

frequent immunologic checks are needed if the hazards of spontaneous infections are to be recognized and avoided.

With the exception of the work of Grace and Suskind,[4] most of the experimental inoculations with pemphigus materials have been made in rabbits. It is well known that these animals are prone to infection with a protozoan parasite, Encephalitozoon cuniculi, and that latent infections of the central nervous system may be lighted up by intracerebral inoculations with foreign material or even by simple puncture. This parasite is cosmopolitan in distribution, and most stocks of domestic rabbits become infected at one time or another. The presence of E. cuniculi is not revealed by aerobic or anaerobic cultural methods, and the organism is readily transmitted serially from brain to brain. Hence, the unwary investigator may be led to believe that he is dealing with a virus etiologically related to the disease under investigation. If filtrates fail to transmit the disease as readily as crude tissue emulsions, it is natural to invoke the well known facts that some viruses filter with great difficulty and that the process of filtration may greatly reduce the amount of virus in potent emulsions.

In spite of its name, E. cuniculi is primarily a kidney parasite. This fact was brought out by the work of Smith and Florence [5] and by the earlier observations of Twort and Archer,[6] who believed that they were dealing with a nephritis caused by a filtrable virus. The latter investigators described the symptoms, the lesions in the brain, the progressive cachexia and even the alopecia which constitute the current syndrome of experimental pemphigus in the rabbit. (In the years immediately following the World War, these same manifestations were thought to characterize human lethargic encephalitis in the rabbit.) In 1924, Da Fano [7] reviewed the literature concerning spontaneous encephalitis in rabbits and pointed out a number of instances in which this protozoan infection had led to confusion and erroneous conclusions on the part of investigators who failed to recognize the disease.

It seems likely that the agent described by Grace and Suskind [4] also belongs in the category of spontaneous infections, although it is clear that they are not dealing with the protozoan parasite studied by Cowdry

4. Grace, A. W., and Suskind, F. H.: An Agent Transmissible to Mice Obtained During a Study of Pemphigus Vulgaris, Proc. Soc. Exper. Biol. & Med. **37**:324, 1937.

5. Smith, T., and Florence, L.: Encephalitozoon Cuniculi as a Kidney Parasite of the Rabbit, J. Exper. Med. **41**:25, 1925.

6. Twort, C. C., and Archer, H. E.: The Experimental Production of a Fatal Nephritis with a Filter Passing Virus of Nervous Origin, Lancet **1**:1102, 1923.

7. Da Fano, C.: Spontaneous and Experimental Encephalitis in Rabbits, M. Science **10**:355, 1924; Protozoan-like Parasites in Spontaneous Encephalitis of Rabbits, J. Path. & Bact. **27**:333, 1924.

and Nicholson [8] which closely resembles or is identical with E. cuniculi. Grace [9] has stated the belief that his virus is not the same as that described by Urbach and that rabbits are unaffected by the agent which he isolated from mice. In the discussion of their most recent publication, Grace and Suskind [9] stated that mice recovered from infection were not found to be resistant to reinfection by the same agent. This is the only immunologic work they have reported. They apparently have not attempted neutralization tests with pemphigus patients' serum to establish some relationship between their virus and the human disease. The agent with which they are dealing appears to be decidedly pyogenic. This property is in no way reflected in the pathologic changes of human pemphigus. On the other hand, the massive polymorphonuclear infiltrations in their mice are suggestive of the action of a virus recently described by Woglom and Warren.[10] This virus was isolated from rats, but it is also pathogenic for mice.[10a]

In the writings of Urbach and Wolfram,[11] considerable emphasis is laid on the suboccipital route of inoculation. While this method may offer certain advantages, these are largely offset by the opportunity it presents for serious trauma. Moreover, it would seem improbable that virus introduced directly into nerve tissue by cerebral injection would fail to infect whereas it would do so if inoculated suboccipitally into the dural spaces. By either method, most of the inoculum doubtless finds its way into the cerebrospinal fluid. Fleck and Goldschlag [12a] recently reported an interesting experiment in which they had the opportunity to observe the effects of trauma under what might be called optimum conditions. Since they were dissatisfied and unconvinced by the results of their own inoculations, Dr. Wolfram volunteered to

8. Cowdry, E. V., and Nicholson, F. M.: Coexistence of Protozoan-like Parasites and Meningoencephalitis in Mice, J. Exper. Med. **40**:51, 1924; Meningoencephalitic Lesions and Protozoan-like Parasites in Brains of Apparently Normal Laboratory Animals Commonly Employed for Experimentation, J. A. M. A. **82**:545 (Feb. 16) 1924.

9. Grace, A. W., and Suskind, F. H.: An Investigation of the Etiology of Pemphigus Vulgaris: The Isolation of a Transmissible Agent from a Fourth Case of the Disease, J. Invest. Dermat. **2**:1, 1939.

10. Woglom, W. H., and Warren, J.: A Pyogenic Virus in the Rat, Science **87**:370, 1938.

10a. Since this paper was submitted for publication it has been discovered that this filtrable agent is a cultivable micro-organism belonging to the bovine pleuropneumonia group.

11. Urbach, E., and Wolfram, S.: Virus of Pemphigus and Dermatitis Herpetiformis, Arch. Dermat. & Syph. **33**:788 (May) 1936.

12. Fleck, L., and Goldschlag, F.: (*a*) Further Experimental Studies on Pemphigus, Brit. J. Dermat. **51**:70, 1939; (*b*) Experimentelle Beiträge zur Pemphigusfrage, Klin. Wchnschr. **16**:707, 1937.

perform the injections for them at the Lwów Clinic. Thirty-four rabbits were inoculated, and 23 of these rabbits received normal blood serum or other material of nonpemphigus origin. In 3 animals among the pemphigus test group and in exactly the same number among the controls Urbach's paralysis developed, and they died. Postmortem examination of the controls revealed unmistakable evidence of trauma to neural and vascular tissue in the region of the fourth ventricle. Fleck and Goldschlag came to the conclusion that this method of inoculation is a dangerous one and that animals may die as a result of trauma several days after the inoculation is made. Since Urbach and Wolfram regarded the death of any animal forty-eight or more hours after inoculation as resulting from pemphigus virus infection, their high percentage of successful inoculations becomes more understandable.

In addition to animal transmission experiments, Urbach and his colleagues have offered a certain amount of serologic and immunologic evidence designed to show the relationship of their virus to human pemphigus and to other viruses. Although Urbach, Wolfram and Brandt [13] described a complement fixation reaction which appeared to have prognostic as well as diagnostic value, Fleck and Goldschlag [12] found that the test was lacking in specificity, since 25 per cent of syphilitic serums gave a positive reaction with the antigen prepared by the Viennese investigators. Moreover, they observed that serums giving a positive reaction with the pemphigus rabbit brain antigen reacted in the same manner with phenolized normal rabbit brain as well as with phenolized starch or malt solutions.

The relationship of rabies virus to Urbach's rabbit pemphigus virus, described by Schweinberg and Wolfram,[14] is unconvincing. Their published protocols show that not only did serums from patients with pemphigus and dermatitis herpetiformis neutralize their rabies virus but so did their control serums from patients with herpes zoster, erythema exudativum multiforme, mycosis fungoides, erythema annulare and Darier's disease. A strain of rabies virus susceptible to neutralization by serums from such diverse sources is certainly of doubtful value in establishing serologic relationships.

Our single experiment using pemphigus blister fluid as a major part of the medium in the culture of chick tissues has a bearing not only on the possible infectious nature of pemphigus but also on the validity of the Pels-Macht test. It would seem reasonable to suppose that a specific

13. Urbach, E.; Wolfram, S., and Brandt, R.: Zur Serodiagnose des Pemphigus, Klin. Wchnschr. **15**:1479, 1936.

14. Schweinberg, F., and Wolfram, S.: Ueber serologische und immunologische Beziehungen zwischen den Erregern des Pemphigus und der Lyssa, Ztschr. f. Immunitätsforsch. u. exper. Therap. **91**:341, 1937.

substance of mammalian origin sufficiently toxic to inhibit the growth of a plant seedling would also have a decidedly toxic effect on naked animal cells growing in tissue culture. On the contrary, our cultures containing relatively high concentrations of blister fluid grew as luxuriantly as did those in normal rabbit serum. On statistical grounds, Sansome and Forman [15] and Hollander and Greb [16] have also cast doubt on the validity of the phytopharmacologic test of Pels and Macht in the diagnosis of pemphigus.

SUMMARY AND CONCLUSIONS

Experiments are described in which it was attempted to demonstrate the presence of a filtrable virus in pemphigus blister fluid by the inoculation of the chorioallantoic membrane of the developing chick and by intracerebral inoculation of rabbits and irradiated mice. The results were entirely negative.

On the basis of clinical and experimental data, it is concluded that there is insufficient evidence at present to justify the theory that a virus is the cause of pemphigus vulgaris.

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15. Sansome, F. W., and Forman, L.: A Note on the Phytopharmacological Index in Pemphigus, Brit. J. Dermat. **51**:63, 1939.

16. Hollander, L., and Greb, R. J.: Evaluation of the Phytopharmacologic Test of Pels and Macht, Arch. Dermat. & Syph. **33**:1012 (June) 1936; Further Report, ibid. **34**:650 (Oct.) 1936.

ABSORPTION OF ROENTGEN RAYS BY THE SKIN

EXPERIMENTAL DETERMINATIONS

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The biologic effect of roentgen irradiation depends on absorption of the rays applied to the site of the pathologic process. In different cutaneous lesions this site is situated at different levels in the skin and subcutaneous tissues; hence it is necessary to determine the optimal quality and quantity of radiation to use in each specific case. It was therefore deemed advisable to determine the amount of radiation of the qualities used in dermatologic practice which is absorbed in successive millimeters of skin.

MATERIAL AND METHOD

Determinations of absorption were made with live and dead rabbit skin, ear and thigh, fresh human skin obtained from the operating room, water and aluminum. Our measurements were all made in air, to avoid the effect of scattering. The apparatus used was a mechanical rectifier with a universal type Coolidge tube. The peak kilovoltage was 100, the milliamperage was 3 and the skin focal distance was 50 cm., with a portal 3 by 3 cm.

Since the amount of scattering is dependent on many factors, we attempted to determine to what degree the freely circulating blood influences scattering. A white rabbit was securely tied to a board, and the hair was clipped from an area measuring 9 by 9 cm. A double thickness of skin was held together with clamps, measured and exposed to a beam of roentgen rays. The dose delivered to the surface was 57 r per minute. The same dose was applied to the ear and to the fleshy part of the thigh, and in each case the transmitted portions of the roentgen beam were measured. The animal was then anesthetized, and a flap of skin was cut sufficiently large to cover the ionization chamber. There was no interference with the free circulation of the blood. A reading was taken, and the thickness of the skin was measured with a micrometer. Finally the animal was anesthetized and killed, the flap of skin was removed and the ear and thigh were severed. The amount of radiation absorbed by these dismembered parts was measured. The experimental conditions and the thicknesses of the test materials were not altered.

We were interested only in comparing the absorption by live and by dead tissues, so that the effect of circulation could be definitely determined. Table 1 clearly indicates negligible difference in absorption between live and dead tissues. The conclusion is justifiable that for small thicknesses and for small areas the

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Read at the Sixty-Second Annual Meeting of the American Dermatological Association, Inc., Monte-Bello, Quebec, Canada, June 1, 1939.

amount of absorption of a low voltage x-ray beam is not measurably influenced by normal circulation.

The absorption of radiation in human skin was next determined. The same factors, apparatus and conditions were used for these experiments as for those with animal tissues. Having determined that freezing of human skin with solid carbon dioxide has no effect on absorption of the roentgen rays, we cut the skin in thicknesses of 1 mm. Fresh human skin was obtained from the operating room. Care was taken to prevent evaporation of water. Not only was the subcutaneous tissue separated from the skin, but the cutis was cut away from the epidermis. The thickness of the skin and that of the fat were measured by placing each on a glass slide and placing another slide carefully over the surface of the material. The thickness of the specimen minus that of the slides was determined with a micrometer. We thought that this would be more accurate for our purpose than weighing a known area. The skin, cut into convenient sizes, was placed over a piece of lead foil having an appropriate opening. A tripod was used to support the lead foil and the sample in such a way that the x-ray tube was directly over, and the ionization chamber directly below, the skin. Absorption readings obtained

TABLE 1.—*Relative Transmission of Low Voltage Unfiltered Roentgen Rays in Live and in Dead Animal Tissue*

	Thickness of Tissue	Dose Applied to Surface, r/Min. in Air	Transmission in Live Tissue, r/Min.	Transmission in Dead Tissue, r/Min.
Double thickness of rabbit skin	3.6 mm.	57	31.2	31
Rabbit skin flap	1.7 mm.	57	42	41.4
Rabbit ear	1.2 mm.	57	45.2	44.8
Rabbit thigh	3.3 cm.	57	11	11

with varying thicknesses of human skin and fat were compared with those obtained with rabbit skin, water and aluminum. These data appear in table 2 and figure 1.

It is interesting to note that the skin absorbs a greater percentage of the incident beam than does its underlying subcutaneous tissue or water. However, when averages of the absorption readings for fat and skin are obtained, pooled and compared with those for water the difference is negligible. There is general agreement that the density of water and that of human tissues are about the same, and therefore experimental results obtained with a water phantom apply to human tissues. In this study, clipped rabbit skin absorbed more radiation than did human skin or water.

In order to measure the degree of absorption of an x-ray beam by successive small thicknesses of water, an apparatus was devised for this purpose. If we had placed an ionization chamber in a water tank as one would do in performing water phantom experiments, the interference by scattering would have been so great as to invalidate our results for comparison. The cylinder and plunger arrangement shown in figure 2 was utilized. The plunger was attached by a side arm to a set screw which measured 12 full turns per centimeter of plunger motion. Therefore, each turn of the set screw increased by 0.83 mm. the column of water which the roentgen rays had to traverse. The cylinder and plunger were made of bakelite tubes with paper across the bottom which was stiffened and waterproofed with a cellulose cement. This paper absorbed only about 2 per cent of the incident beam, but the water which seeped under the plunger absorbed about 15 per cent. A reading was obtained with each successive turn of the set screw. The data are shown in table 3.

The device was supported on a tripod with the x-ray tube above it. The diaphragm emitted a pencil of rays which traversed the hollow plunger and the column of water beneath it and finally struck the ionization chamber placed

TABLE 2.—*Comparative Absorption of Low Voltage Unfiltered Roentgen Rays in Varying Thicknesses of Different Materials*

Human Skin		Human Fat		Rabbit Skin		Water		Aluminum	
Mm.	r/Min.	Mm.	r/Min.	Mm.	r/Min.	Mm.	r/Min.	Mm.	r/Min.
0	45.2	0	44.4	0	57	0	38	0	61.8
2.0	33.6	10	21.6	1.7	42	2.5	28	1	25.2
4.25	25.2	18	14.8	3.6	31.2	5.0	23.6	2	17.6
6.40	21.2	26	12.0			7.5	20.7	3	15.0
8.35	17.6					10.0	18.0	4	12.0
						12.5	15.9	5	11.0
						15.0	14.5	6	9.6

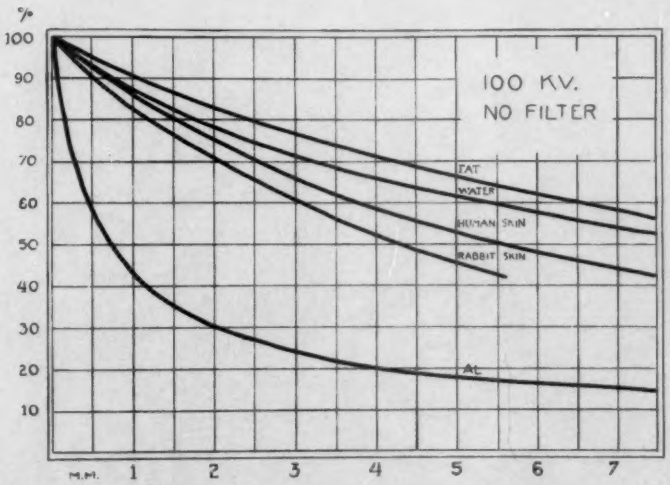

Fig. 1.—Curves representing absorption by various test materials used in our experiments of roentgen rays with unfiltered radiation at 100 kilovolts.

beneath the water device. This arrangement eliminated scattering for the most part.

Absorption curves for aluminum were obtained in the conventional manner, whereby primary absorption only is measured. It was our aim to measure all data under equal conditions in order to permit direct comparison of the absorption measurements through various substances.

So far we have determined (1) that there is a negligible difference in absorption between live and dead tissue that has not been subjected to loss of fluid; (2) that there is a definite difference in absorption between rabbit and human skin and that this difference can be calculated mathematically, and (3) that there is agreement in absorption readings between skin with its subcutaneous tissue and water. These experiments open the way to further and more accurate studies on the absorption of roentgen rays in minute thicknesses of cutaneous structures.

The next phase of the study was concerned with the relative absorption of rays of different qualities by water and by human skin. Aluminum was used both as a control and for comparative purposes. Absorption curves were made with the irradiation factors previously described, and human skin, water and aluminum were used as filtering materials. The rays used were grenz rays (10 kilovolts) 40, 60, 80, 100 and 115 kilovolts peak, with 3 milliamperes and no filtration; also 137 kilovolts peak, with 5 milliamperes and a 3 mm. aluminum filter. The data are recorded in table 4, and curves obtained from these figures are illustrated in figure 3. It is interesting to note that the higher the voltage

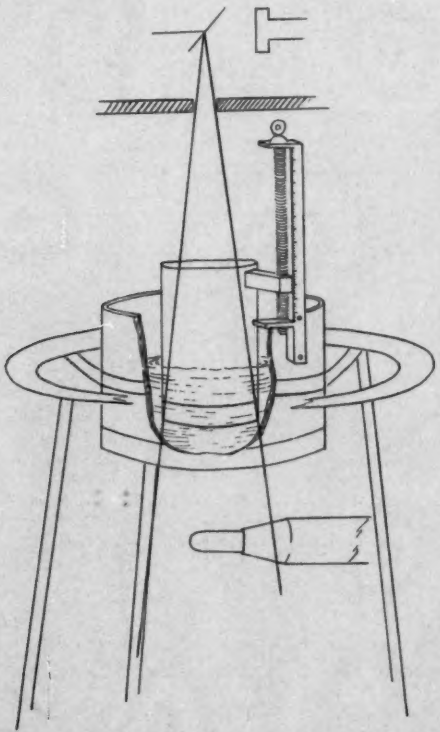

Fig. 2.—Diagram of the apparatus used for measuring the transmission of roentgen rays through water. The tripod holding the device, the relative positions of the x-ray tube, the diaphragm and the ionization chamber are also indicated.

and filtration the greater the transmission of the x-ray beam through skin, water and aluminum. The reverse is true for the lower voltages.

The figures obtained in the absorption experiments were plotted on semilogarithmic graph paper. The purpose of these graphs was to show more specifically the absorption quality of the test materials (human skin, water and aluminum) and also to compare the relative depths of penetration of radiations of varying qualities (10 to 140 kilovolts peak). The results are shown in figure 4.

Thus, the half value layer for 100 kilovolts peak with no filter in skin is about 5.7 mm., whereas in water it is 8 mm. and in aluminum it is about 0.7

mm. It can therefore be said that the amount of absorption for low voltage radiation in aluminum is approximately ten times that in water. Meyer has repeatedly pointed this out. The same relative differences are seen with other voltages.

TABLE 3.—*Relative Absorption of Low Voltage Unfiltered Roentgen Rays in Varying Heights (Thicknesses) of Water*

Material	Absorption, r/Min.	Material	Absorption, r/Min.
Air	47.0	Water—Continued	
Paper	46.0	12 turns	18.0
Water (seeped)	38.0	13 turns	17.1
1 turn*	33.6	14 turns	16.8
2 turns	30.0	15 turns	15.9
3 turns	28.0	16 turns	15.4
4 turns	27.2	17 turns	15.2
5 turns	25.2	18 turns	14.5
6 turns	23.6	19 turns	14.0
7 turns	22.5	20 turns	13.7
8 turns	21.9	21 turns	13.4
9 turns	20.7	22 turns	13.0
10 turns	19.2	23 turns	12.6
11 turns	18.6	24 turns	12.4

* Turns of the set screw in the apparatus shown in figure 2. At each turn the column of water to be traversed by the roentgen rays was increased by 0.83 mm.

TABLE 4.—*Relative Difference in Absorption of Roentgen Rays with Radiations from 10 to 137 Kilovolts Peak in Human Skin, Water and Aluminum* *

	10 Kv. (Grenz)		40 Kv.		60 Kv.		80 Kv.		100 Kv.		115 Kv.		137 Kv. (5 ma. and 3 mm. Al.)	
	Mm.	r/Min.	Mm.	r/Min.	Mm.	r/Min.	Mm.	r/Min.	Mm.	r/Min.	Mm.	r/Min.	Mm.	r/Min.
Skin	0	324	0	9.8	0	22.0	0	34.8	0	45.2	0	54	0	16.4
	1.05	78.0	4.06	4.3	4.06	10.6	4.06	18.5	2.0	38.6	3.01	35	4.06	14.7
	1.43	40.0	7.61	2.8	7.61	7.5	7.61	13.7	4.25	25.2	5.93	25	7.61	13.5
	2.46	3.0	11.23	1.95	11.23	5.5	11.23	10.6	6.40	21.2	9.20	18.5	11.23	12.4
	4.94	0.7	13.72	1.60	13.72	4.5	13.72	8.9	8.35	17.6	13.13	16.0	13.72	11.7
Water	0	112	0	7.0	0	17.2	0	28.8	0	38	0	45	0	16 8
	0.83	2.8	5.0	3.3	5.0	8.8	5.0	15.2	5.0	23.6	5.0	31.5	5.0	15.6
	1.66	0.95	10.0	2.1	10.0	5.7	10.0	10.5	10.0	18.0	10.0	22.7	10.0	14 0
	2.49	0.6	15.0	1.4	15.0	4.2	15.0	8.2	15.0	14.5	15.0	18.4	15.0	12.6
	3.32	0.3	20.0	1.15	20.0	3.2	20.0	6.4	20.0	12.4	20.0	15.2	20.0	11.7
Aluminum	0	324	0	9.8	0	22.0	0	34.8	0	45.2	0	57	0	16.5
	0.26	1.2	0.25	4.8	0.25	11.6	0.25	20.0	0.25	39.6	0.25	35	0.25	16.0
	....	....	0.50	3.0	0.50	8.0	0.50	15.4	0.5	32.4	0.5	27	0.50	15.2
	....	....	0.75	2.5	0.75	6.4	0.75	12.2	1.0	25.2	1.0	22	0.75	14.2
	....	....	1.0	1.7	1.0	4.9	1.0	10.4	2.0	17.6	2.0	14	1.0	14.0
	....	....	2.0	0.75	2.0	2.75	2.0	5.8	....	....	....	..	2.0	12.4

* The curves in figure 3 were made from these data. Ionization meters for measuring accurately grenz ray dosages are not available; therefore the absorption data for grenz rays may have to be revised.

Since our interest is mainly in the skin, we attempted to show to what degree radiation of 10 to 140 kilovolts peak are absorbed in successive millimeters of skin. The absorption data in table 4 were plotted and superimposed on a cross-sectional diagram of the skin with correct dimensions. Figure 5 shows the actual depth doses (read as horizontal distances) of the various radiations. It is therefore a chart directing the selection of qualities of radiation adequate for effective doses at various depths and for the treatment of lesions at such

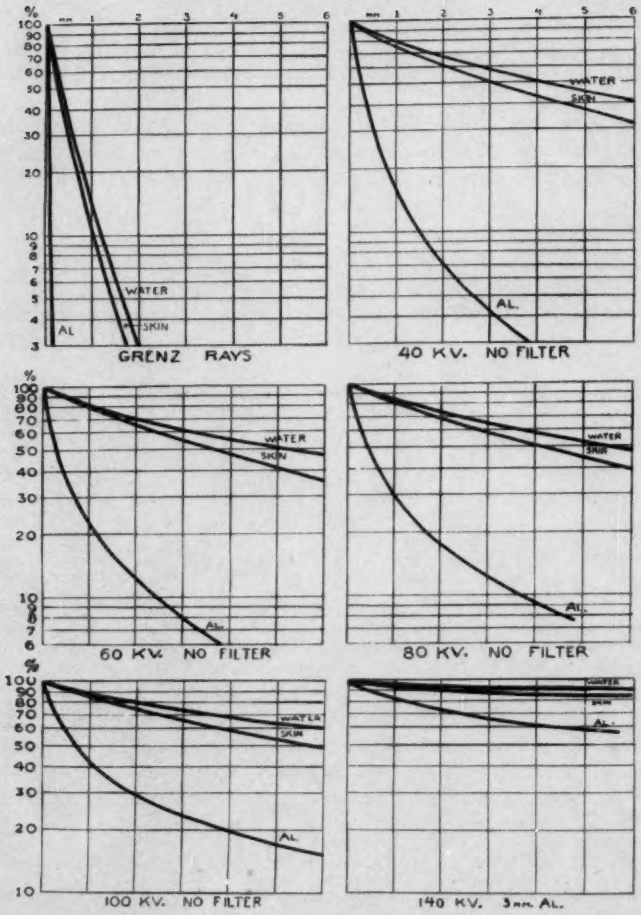

Fig. 3.—Semilogarithmic absorption curves for human skin, water and aluminum with radiations commonly used in dermatology.

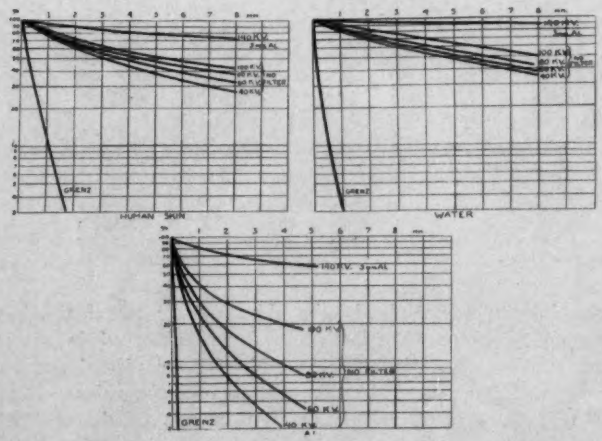

Fig. 4.—Semilogarithmic absorption curves for human skin, water and aluminum with varying voltages. These curves show the relative thicknesses of the different test materials required to absorb a given percentage of radiation.

depths. The diagram illustrates several interesting points which we wish to emphasize. They are:

1. Grenz rays are absorbed except for about 15 per cent of the intensity in the first millimeter of skin.

2. Radiations of 40 to 100 kilovolts peak show differences of absorption of only about 16 per cent at a depth of 6 mm.; at a depth of 3 mm. the difference is only about 10 per cent. This tends to show that for dermatologic roentgenotherapy with nonfiltered radiation rays the lower voltages (40 kilovolts) should be practically as effective as the higher (100 kilovolts).

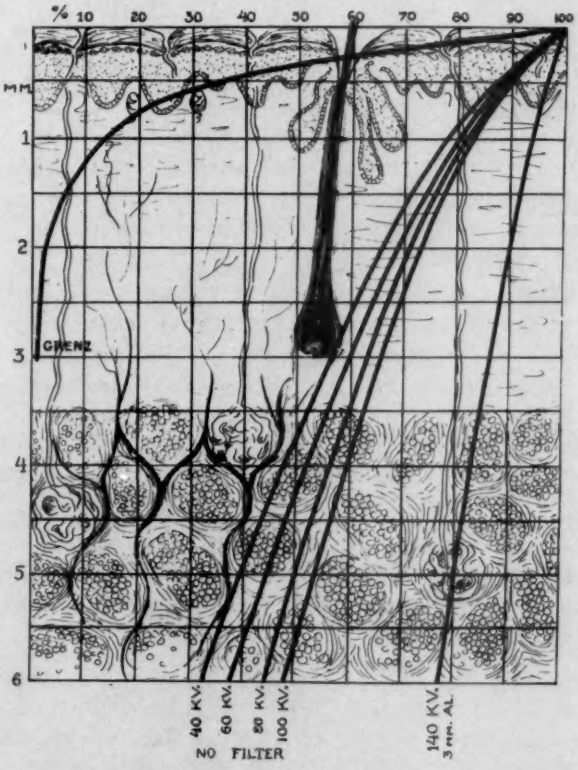

Fig. 5.—Absorption curves showing depth doses of various radiations used in dermatologic practice superimposed with correct dimensions over a cross-sectional diagram of the skin.

3. Filtered high voltage radiations (137 kilovolts peak and a 3 mm. aluminum filter) are very penetrating. At the 3 mm. level there is an absorption of 13 per cent of the incident beam, and at a depth of 6 mm. the absorption is only 22 per cent.

4. The half value layer in skin for varying voltages may be read directly from the diagram. Thus, for grenz rays it is 0.35 mm., for 40 kilovolts it is 3.7 mm., for 60 kilovolts it is 4.2 mm., for 80 kilovolts it is 5.0 mm., for 100 kilovolts it is 5.57 mm. and for 137 kilovolts with a 3 mm. aluminum filter it is 20.5 mm.

COMMENT

The measurement of depth doses has interested radiotherapeutists for many years. Isodose charts are available for treating lesions at any depth. These, however, are of little value to dermatologists because they deal with large thicknesses of tissues. Meyer's [1] article contains interesting and valuable charts dealing with depth doses and qualities of radiation. The data presented by Andrews and Braestrup [2] were based on experiments performed with photographic film. Our work was done with an ionization meter of the thimble type which was standardized in terms of readings of a standard chamber.

Roentgen doses expressed in international roentgens give little information regarding the biologic reaction. All reactions to the roentgen rays are atomic reactions and consist in the change of a neutral atom into an ion. As a result, chemical reactions take place in the cell, which produce biologic changes. The extent of the biologic changes depends not only on the duration of the irradiation and on the intensity of radiation which reaches the lesion but also on that portion of the radiation which is absorbed in the unit volume of the lesion. There is a definite difference in cutaneous reactions with different qualities of radiation. There have been many articles written to show this difference, including the two by MacKee and Cipollaro.[3] The effect of radiation is influenced by its quality. The number of roentgens applied to the surface is no indication of what goes on deep in the tissues. Filtered high voltage radiation produces biologic reactions quite different from those produced with unfiltered low voltage radiation, even though the surface effect, that is, the erythema or the effect on a few layers of cells (Drosophila eggs), may appear to be the same. In spite of these differences, it is advisable for practical therapeutic purposes to express physical measurements in terms of biologic reactions.

CONCLUSIONS

1. For small areas and for small thicknesses of animal skin (1 to 4 mm.) the freely circulating blood does not increase or decrease absorption of the roentgen rays to any appreciable extent.

2. For superficial irradiation of human skin, the data obtained with dead tissue can be applied to living tissue.

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1. Meyer, W. H.: The Co-Relation of Physical and Clinical Data in Radiation Therapy, Radiology **32**:23 (Jan.) 1939.

2. Andrews, G. C., and Braestrup, C. B.: Measurements of the Depth Dose for Roentgen Therapy Used in Dermatologic Practice, Arch. Dermat. & Syph. **33**:446 (March) 1936.

3. MacKee, G. M., and Cipollaro, A. C.: The Roentgen Unit in Dermatology, Arch. Dermat. & Syph. **30**:761 (Dec.) 1934; Roentgen Dosage in Dermatology Expressed in International Roentgens, ibid., this issue, p. 1.

3. Freezing of dead human skin with solid carbon dioxide does not alter absorption when low voltage radiation is used.

4. Absorption data obtained with water are directly applicable to live human skin.

5. Curves representing absorption with radiations of 40 to 100 kilovolts peak show slight differences up to a depth of 2 mm. It can be assumed, therefore, that lesions situated at this level can be equally affected by a quality of radiation between 40 and 100 kilovolts peak.

6. Grenz rays are sufficiently penetrating to be of some value in the treatment of lesions situated within the first 0.5 mm. of skin. Lesions over 1 mm. in thickness are not effectively influenced by grenz rays.

7. Filtered roentgen rays (137 kilovolts with a filter of 3 mm. of aluminum) are much more penetrating than unfiltered rays and deliver large doses to lesions at considerably greater depths.

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ABSTRACT OF DISCUSSION

Dr. Donald M. Pillsbury, Philadelphia: Much credit is due Dr. Cipollaro and Dr. Mutscheller for this presentation, because although dermatologists employ roentgen rays extensively in therapy, they have not, with a few notable exceptions, contributed as much to the experimental aspect of roentgen therapy as have the radiologists. Certain considerations arise in one's mind in attempting to apply Dr. Cipollaro and Dr. Mutscheller's interesting findings to clinical practice. These become the more important if one approaches a more truly superficial type of roentgen therapy. First, I should like to ask whether any evidence exists concerning varying absorption by the different layers of the skin of roentgen rays of the relatively long wavelength used in these experiments. This might be particularly important in treating conditions in which the stratum corneum is thickened and in which a major portion of the radiation might be absorbed in a region which is physiologically inactive. Second, the inherent filtration of the particular tube which is being used must be considered. Tubes vary greatly in this regard, and it must be kept in mind that even though the same kilovoltage is used roentgen rays of rather different quality may be emitted from different tubes. With a tube with a low inherent filtration, the proportion of rays of long wavelengths would be higher and the effects might even be more superficial than Dr. Cipollaro and Dr. Mutscheller obtained with the tube used in their experiments. It seems to me that this is a matter of great practical significance.

Dr. George C. Andrews, New York: I was particularly interested in hearing this paper because it is along the same lines as one I read two or three years ago on the measurement of the depth dose of roentgen rays in millimeters below the surface of the skin (Andrews, G. C., and Braestrup, C. B.: Arch. Dermat. & Syph. **33**:446 [March] 1936). For our experiment, Dr. Braestrup and I used tissue fresh from the operating room and animal tissue. We found that we were unable to overcome loss of moisture, which made that method inaccurate. Because the tissue dried up, we gave up the use of tissue and found

the photographic film method best. We also thought that the inclined filter method we described was more reliable and accurate than the use of an absorption chamber. For the frame filter method with a water phantom, the filter is arranged at an inclined angle in a water bath and irradiation applied over that; the effect is measured at 1, 2 and 3 mm. up to 15 mm. depth. Our measurements by this method when rechecked were more satisfactory than when we used tissue. Dr. Cipollaro and Dr. Mutscheller tried to avoid back scattering in their measurements. There are some good reasons for doing that. The definition of a roentgen does not include back scattering. But in dealing with skin, we always have back scattering in the tissues which are exposed. Our method included back scattering. The condition is therefore as it actually is in the skin. I think that further work along these lines is desirable.

Dr. George M. MacKee, New York: I wish it were possible to discuss in this connection the advantages and disadvantages of filtered radiation as compared with what is generally called unfiltered irradiation. In the future all radiation used by dermatologists will be filtered, although it will probably be called unfiltered. Shock-proof apparatus is undoubtedly the equipment of the future. Filtration with such apparatus is roughly the equivalent of 0.5 mm. of aluminum. Dr. Pillsbury mentioned an important fact, namely, that the inherent radiation is filtered by the glass wall of the tube. In the past there was considerable variation in the thickness of the wall and therefore in the filtration. For this reason the output varied over 50 per cent. Some of the old tubes caused as much filtration as does the shock-proof apparatus. Modern tubes do not vary in wall thickness. What Dr. Cipollaro and Dr. Mutscheller have attempted to do was to determine absorption in millimeters and loss of tissue more accurately than has heretofore been possible. In this work I was much surprised, as was pointed out, at the slight difference in absorption at 40 kilovolts and 60 kilovolts. It is proper to criticize this article on the basis of possible error. I do not know what the experimental error may be, but I believe it to be slight. Dr. Cipollaro has consulted physicists, physiologists and biochemists in an effort to make the work as accurate as possible, and all said that it is as accurate as it can be at present. I think that it is sufficiently accurate for practical purposes. From this work a little more is learned about the selection of the quality of radiation in so far as it can be selected for lesions at various thicknesses and various depths.

Dr. Earl D. Osborne, Buffalo: I gathered from the charts that there was considerable difference in the amount of absorption between 60 or 70 kilovolts and 100 kilovolts. I should like to ask as a matter of practical treatment whether Dr. Cipollaro feels that it is desirable for a dermatologist treating lesions not deeper than 2 or 3 mm. to use 100 kilovolts rather than 60 to 70 kilovolts. In my personal experience I have a feeling that 70 kilovolts for practical purposes in treating cutaneous conditions is a maximum that one need not exceed, and my results at least seem better with 70 kilovolts than with a higher dose, and there is less danger of deeper effects. I use shock-proof apparatus and have had the manufacturer grind down the windows so that they are equivalent to 0.5 mm. of aluminum. There was an inherent filtration of 1.2 mm. of aluminum in the tube as it came out.

Dr. Anthony Cipollaro, New York: Dr. Pillsbury asked whether there is a difference in absorption in the different layers of the skin. Yes, there is. We determined this experimentally and found that the epidermis, cutis and subcutaneous tissues absorbed varying percentages of the incident beam. The fat absorbed less

radiation than the skin. Absorption curves obtained with epidermis, cutis and fat were compared with those obtained through rabbit skin, rabbit ear and water. It was found that rabbit skin absorbed more radiation than human skin. The inherent filtration of the glass wall of the tube cannot be eliminated. A Coolidge tube was used in our experiments. My understanding is that at present the thickness of the glass wall of all modern Collidge tubes is about the same. With modern shock-proof apparatus used for superficial therapy, there is an inherent filtration equivalent to approximately 0.5 mm. of aluminum.

Dr. Andrews brought up the question of loss of moisture from operating room specimens which were used in our experiments. We avoided this loss in two ways: first, by doing experiments on the same day that the human skin was obtained and, secondly, by putting the specimens in a Ball jar which contained a piece of moist gauze and was tightly closed. This prevented evaporation. Therefore, the specimens of human skin which we used had suffered no loss of water.

Dr. Andrews and Dr. Braestrup performed similar experiments several years ago, but they measured differences in intensity with photographic film. The obvious objections to this method were enumerated in my discussion of their paper. In our experimental work we avoided back scattering because we were interested only in the absorption of an incident x-ray beam without the effect of scattering. Therefore, in the absorption experiments through water our special device permitted us to measure the transmission of an x-ray beam through a column of water of varying thicknesses. The figures that we obtained measured the quantity of the x-ray beam which was transmitted without the effects of back scattering.

Dr. MacKee spoke about filtration. Our absorption curves show that for ordinary superficial lesions filtration is not necessary. Lesions up to 5 mm. in thickness should theoretically respond to treatment with roentgen rays of 40 as well as 100 kilovolts. We shall conduct carefully controlled clinical experiments with these lower voltages and shall report our results in a future communication.

DISEASES OF THE NAILS

REPORT OF CASES OF ONYCHOLYSIS

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There is considerable evidence that diseases of the nails, excluding the pyogenic and fungous infections and changes associated with the inflammatory dermatoses, are often produced by endocrine dysfunction, particularly hypothyroidism and hypopituitarism. There is a definite relation between some dermatologic conditions and the endocrine glands. The influence of the hormones on development and function of the skin, hair and nails is well established. In the past five years I have observed more than 30 cases of spontaneous separation of the nails, in a large portion of which there were symptoms indicative of hypothyroidism and a lowered basal metabolic rate. The majority of the patients have improved on medication with thyroid. In a few cases relapse has occurred with the development of new separations of the nails after thyroid medication was discontinued.

Diseases of the nails are many times overlooked, and careful attention to the nails will often be found a valuable aid to both the dermatologist and the general practitioner in the diagnosis of systemic diseases. Some indication of the frequency of ungual involvement may be obtained from reports such as that of White,[1] who observed 485 cases of diseases of the nails. Pardo-Castello [2] observed 464 patients, 192 (41.37 per cent) of whom had abnormal nails. The nails were affected by the same conditions that attack the general surface of the skin. Many cutaneous diseases produce ungual symptoms. General systemic diseases, such as the anemias, avitaminosis and the endocrine disturbances, may present important changes of the nails.

White [1] in his report of 485 cases of diseases of the nails found that 141 patients had onycholysis. The condition in 24 of these was associated with eczema, in 15 with trauma, in 21 with panaritium, in 37 with psoriasis, in 11 with syphilis and in 11 with fungous

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From the Department of Dermatology and Syphilology, Baylor University, College of Mediciine.

Read at the Sixty-Second Annual Meeting of the American Dermatological Association, Inc., Monte-Bello, Quebec, Canada, June 1, 1939.

1. White, C. J.: Clinical Study of Four Hundred and Eighty-Five Cases of Nail Diseases, Boston M. & S. J. **147**:537 (Nov.) 1902.

2. Pardo-Castello, V.: Diseases of the Nails, South. M. J. **27**:377 (May) 1934.

diseases. However, he apparently did not limit his cases to those of spontaneous separation of the nail from its bed.

The term onycholysis should be used in a more restricted sense, designating only spontaneous separation. The progress of the disease is usually gradual, beginning at the lateral free border of the nail and gradually increasing, with separation of the nail from the nail bed and the development of a space which may at times be filled with debris. The separation may be slight, but it frequently increases until the anterior half or two thirds of the nail is raised from the nail bed and occasionally until the nail is separated from its attachment at the matrix and is easily removed or shed. The surface of the nail is smooth, and there is no inflammatory process of the paronychium. The entire process is painless, and the separation remains over a long period, or there is improvement and regression. At times the nails become entirely normal, and after weeks or months recurrence takes place. There are fewer case reports of onycholysis in the literature than of almost any other condition of the nails.

Pardo-Castello [3] reported cases of onycholysis from syphilis, eczema, psoriasis and anemia and others in which the cause could not be ascertained. Strauss [4] reported 1 case of onycholysis and 1 of onychomadesis. Chargin [5] reported a case of typical onycholysis "idiopathica" which developed during pregnancy and increased after term. He described the typical separation beginning at the free margin and gradually increasing until a third or more of the nail was involved. Templeton [6] has reported 5 cases of separation of the nails of young women as an industrial disease related to the washing of paste from bottles. Viecelli [7] observed the condition in a tanner who soaked his hands in brine. Heller [8] examined 562 patients with endocrine disturbances and found only 8 instances of ungual disease of glandular origin. In his monograph [9] he described 10 cases of onycholysis of indefinite causation and stated that in the literature there are reports of 40 or 50 cases of endocrine disturbances with pathologic changes of the nails, in 16 of

3. Pardo-Castello, V.: Diseases of the Nails, Springfield, Ill., Charles C. Thomas, Publisher, 1936, p. 142.

4. Strauss, M. J.: Onycholysis and Onychomadesis, Arch. Dermat. & Syph. **26**:644 (Oct.) 1932.

5. Chargin, L.: Onycholysis Idiopathica, Arch. Dermat. & Syph. **21**:1051 (June) 1930.

6. Templeton, H. J.: Onycholysis, J. A. M. A. **97**:1950 (Dec. 26) 1931.

7. Viecelli, J. D.: Onycholysis, Arch. Dermat. & Syph. **33**:697 (April) 1936.

8. Heller, J.: Onychopathologie und Endokrinologie (nach Beobachtung an 562 Fällen endokriner Störungen), Deutsche med. Wchnschr. **52**:786 (May) 1926.

9. Heller, J.: Die Krankheiten der Nägel, Berlin, Julius Springer, 1927, pp. 113 and 308.

which there was some type of dysfunction of the thyroid. The nails were described as atrophic, dystrophic, hypertrophic, dry, fragile, lusterless, thickened, irregular, slow growing and opaque.

This report is based on the study of 30 cases of abnormality of the nails, some of which were not followed sufficiently to give accurate final observations. Of the 30 patients, 28 were women and 2 were men. Twenty-seven had multiple separations, and 3 had separation of a single nail. Twenty had low basal metabolic rates, and 15 of these had other symptoms suggesting hypothyroidism, such as a tendency to gain weight easily, a requirement of eight to ten hours' sleep, easy fatigability, excessive susceptibility to cold weather, dryness of the skin and hair and brittle nails. Several had what I termed winter pruritus (pruritus hiemalis), with dryness of the skin over the entire body and in cool weather annoying itching, which was aggravated by frequent bathing. The skin usually assumed a normal appearance in warmer weather. One patient had psoriasis of the elbows, but there was no evidence of psoriasis of the nails; another had lichen planus without any inflammatory process of the nails, and 1 had recovered from lichen planus several months previously. Twenty-one showed improvement on thyroid medication, 3 did not improve and 3 were not observed for a sufficient period to

Fig. 1 (case 5).—Separation of all the nails of both hands except that of the left index finger. The basal metabolic rate was —13 per cent. The nails became normal after thyroid medication.

Fig. 2 (case 3).—Separation of the nail of the right ring finger. The nail was removed surgically, but separation developed after regrowth. The separation improved and recurred. After thyroid medication the separation disappeared, and the nail has remained normal.

Fig. 3 (case 11).—Symptoms suggesting mild hypothyroidism. The basal metabolic rate was + 11 per cent. The nails were entirely normal at the end of five months with 2 grains (0.13 Gm.) of thyroid extract daily.

determine the final results. The separation developed in 1 case while the patient was taking 10 grains (0.65 Gm.) of thyroid daily, and the basal metabolic rate was found to be + 15 per cent. The nails improved rapidly when thyroid was discontinued. One patient had had symptoms suggesting hyperthyroidism ten years previously and improved with iodine medication, but at the time of the nail separation the basal metabolic rate was — 12 per cent and there were definite symptoms of hypothyroidism. Two patients had multiple separations from chemical irritation. In 3 patients an unexplainable factor was observed, in 1 case by Shelmire [10] and in 2 by me, in which there was a definite history of acute exacerbation of the nail separation, evidenced by tenderness and a 1 to 2 mm. horizontal erythematous inflammatory band

Fig. 4 (case 30).—Eczematoid dermatitis of terminal phalanx of each finger with extensive nail separations produced by irritation from permanent waving fluid.

adjacent to the line of separation, which developed within twenty-four hours and lasted one or two days after the ingestion of alcohol.

Marie and Woringer [11] reported a case of koilonychia associated with acrocyanosis and hyperhidrosis. Mixed glandular therapy resulted in the development of normal nails. Wander [12] observed a girl aged 9 years with dry, brittle nails, scanty hair, hyperkeratoses of the fingers and toes and painful palmar hyperkeratoses. The nails were thickened

10. Shelmire, B.: Personal communication to the author.

11. Marie, G., and Woringer, F.: Un cas de koïlonychie: Guérison après traitement par un extrait pluriglandulaire, Bull. Soc. franç. de dermat. et syph. **37**: 1214 (Dec.) 1930.

12. Wander, W. G.: Dystrophy of the Finger Nails and Toe Nails (Spoon-Nails), Arch. Dermat. & Syph. **27**:1011 (June) 1933.

Data on Thirty Cases of Abnormal Nails

Case	Patient: Race	Sex	Age	Associated Symptoms	Involvement of Nails	Basal Metabolic Rate	Comment
1	W	F	35	Gains weight easily	Separation of nails of right middle finger and left ring, middle and little fingers	—32	Gradual improvement from 2 grains (0.13 Gm.) thyroid daily; entirely normal nails at end of 5 months
2	W	F	35	Dry skin; freezes; sleeps excessively; tires easily; psoriasis of elbows; no pitting nails	Separation of nails of right ring and little fingers and left little finger, aggravated by ingestion of alcohol	—36	From 2 grains (0.13 Gm.) thyroid daily improved gradually, but condition recurred when thyroid was discontinued during influenza; nails became normal when thyroid was resumed; patient became pregnant
3	W	F	32	Separation of nail; removed surgically but recurred; improved and recurred for 2 years	Separation of nail of right ring finger; recurred 3 months after surgical removal	—26 —21	Improved gradually from 2 grains (0.13 Gm.) thyroid daily; later B.M.R. —2 and nails better than for last 3 years; remained normal
4	W	F	24	Gains weight; freezes; dry skin; sleeps 10 hours	All nails partially separated for 6 months; right index and left middle fingers show 75% separation	—12	Improving from 2 grains (0.13 Gm.) thyroid daily; two nails removed surgically and regrew normally; 1 year required for all nails to become normal
5	W	F	25	Sleeps 10 hours; gains weight; tires easily; hands cold and moist	Separation of nails of right thumb, index, middle, ring and little fingers and of all left fingers except index	—13	2 grains (0.13 Gm.) thyroid daily, nails became normal
6	W	F	20	Freezes in winter; gains weight easily; skin dry	Separation of several nails	—4	Improved rapidly from 1 grain (0.06 Gm.) thyroid daily; no recurrence in 2 years
7	W	F	43	Dry skin, hair and nails; gains weight easily; susceptible to cold; sleeps 8 to 10 hours	For 4 years has had recurrent separations of nails; right thumb nail became complete and was shed 4 years ago; improved from thyroid ¾ grain (0.05 Gm.) daily; separations recur when thyroid is discontinued	—5 (4 yrs. ago)	For several years has improved from small dose thyroid; recent B.M.R. —4; started 1½ grains (0.09 Gm.) thyroid daily, with rapid improvement; condition recurred when thyroid was discontinued
8	W	F	52	Freezing in winter; skin, hair and nails dry; gains weight; palms dry, mildly keratotic; 10 years ago very nervous with rapid pulse; took iodine, with rapid improvement	Nails began to separate 2 years ago and have improved and become worse; right little finger, 90% separation; right middle finger, 75%; right ring finger, 25%; right index finger thickened and dystrophic	—12	Started with ½ grain (0.03 Gm.) thyroid daily and in 3 weeks gradually increased to 2 grains (0.13 Gm.) daily; nails improved rapidly; stopped thyroid because of nervousness; separations recurred
9	W	F	53	Skin dry in winter; sleeps 8 to 10 hours	All nails dry and brittle; more marked last year with longitudinal striations; has had recurrent separation for 5 years; (right little, ring and index fingers and left little, ring and index fingers)	—18	Thyroid gradually increased to 2 grains (0.13 Gm.) daily with improvement of nails after 1 month, which continued; nails normal at end of 2 months

Data on Thirty Cases of Abnormal Nails—Continued

Case	Patient: Race	Sex	Age	Associated Symptoms	Involvement of Nails	Basal Metabolic Rate	Comment
10	W	F	35	Menstrual irregularity for several years; roentgen sterilization	Separation of all nails on right hand and of left thumb, ring and middle finger nails; toe nails also separated	—11	Improved from thyroid and recurred with influenza; fair results on 2 grains (0.13 Gm.) daily but recur from time to time; probably hypopituitary also
11	W	F	24	Freezes; dry skin; excessive sleep; overweight	Separation of nails of right middle and index fingers and thumb and of left middle and index fingers and thumb	+11	2 grains (0.13 Gm.) thyroid daily; nails were improved in 2 months and normal at the end of 5 months
12	W	F	33	Symptoms suggest mild hypothyroidism	Separation of nails of right ring and little fingers and of left little finger	None	Improved with thyroid at end of 2 months; unable to obtain further observation
13	W	F	49	Blood pressure 180/120 to 240/150 for 3 to 4 years; sleeps 9 hours; gains weight; freezes in winter; 7 miscarriages; had 6 roentgen treatments to nails, no improvement	Separation of nails of right index, middle and ring fingers; left thumb and middle and ring fingers	—28	Nails improved slowly; blood pressure dropped to 150/90, lower than in years; 2 grains (0.13 Gm.) thyroid daily; B.M.R. now —8; nails improve and recur and recently on 1 grain (0.06 Gm.) thyroid, but not a satisfactory result
14	W	M	45	No history suggestive of thyroid deficiency	Separation of nails of right middle, ring and little fingers; half separation of all nails on left; nails dark, with some dystrophic changes	—15	Unable to follow results
15	W	M	31	Nails separated 5 years ago and have improved and become worse; mother, 70, has same condition	Separation of all nails on right and of nails of left thumb and index, middle and ring fingers	—5	Slight improvement on high vitamin diet for 1 year and then recurred; 2 grains (0.13 Gm.) thyroid daily produced rapid improvement in 6 weeks then sudden recurrence followed by improvement
16	W	F	34	Drowsy; lethargic; gains weight easily; taking thyroid 3 years for B.M.R. —35; recent excessive menses	Separation of nails of right little and ring fingers; left little and ring fingers; separation increased by alcohol; 10 grains (0.65 Gm.) thyroid daily now	+15	Thyroid stopped; nails rapidly improved, patient feels much better
17	W	F	36	Has had separation of nails for 4 months; B.M.R. low 3 years ago; thyroid taken for some time	Separation of all finger nails and great toe nails	Low 3 yrs. ago	Unable to follow
18	W	F	41	Menses irregular; freezes; skin dry; large doses of arsenic for last year for lichen planus; no evidence of lichen planus of nails	Multiple separation of slight degree	—9	Improved with thyroid ½ grain (0.03 Gm.) daily and were normal in 4 months
19	W	F	52	Lichen planus for 6 months; no inflammatory lesions of nails	Slight separation of several nails at lateral distal edge	—1	Improved rapidly with thyroid, ½ grain (0.03 Gm.) daily; recurrence 1 year later; improved rapidly again on ½ grain (0.03 Gm.) thyroid daily; thyroid continued; nails remained normal

Data on Thirty Cases of Abnormal Nails—Continued

Case	Patient: Race	Sex	Age	Associated Symptoms	Involvement of Nails	Basal Metabolic Rate	Comment
20	W	F	49	Freezes; dry skin; B.M.R. —15 3 years ago; took thyroid for a time	Separation multiple; 1 year ago improved with roentgen therapy; recent recurrence of nail separations	—6	Improved with roentgen therapy and recurred; now taking 2 grains (0.13 Gm.) thyroid daily and improving slowly
21	W	F	44	Gains weight; sleeps 9 hours; nervous; married 22 years; no pregnancies	Separation of right right ring and index fingers for 1 year; index nail removed surgically	—27	Improved slowly with thyroid and ovarian extract; nail removed regrew normally after starting thyroid and other nail became normal in 1 year
22	W	F	37	Dry skin; gains weight; freezes; B.M.R. —24; 1 to 5 grains (0.32 Gm.) thyroid for 1 year but none the last year	Dry, brittle fingernails; two nails separated slightly	—17	Started thyroid with improvement of general symptoms; nails improved rapidly
23	W	F	28	Nails dry and brittle with white spots	Separation of nails of right index and left middle fingers; nails dry, brittle and pitted, with white spots	—10	½ grain (0.03 Gm.) thyroid daily for 1 week; stopped because of nervousness; nails improved with roentgen therapy
24	W	F	22	Sleeps 9 to 10 hours; dry skin; freezes in winter; irregular menses	All nails show early separation with 2 mm. red band at point of separation about distal edge	—8	Unable to get subsequent observation
25	C	F	30	Separation and dystrophy of nails	Separation of nails of right middle and index fingers and thumb; left middle finger and thumb	—15	2 grains (0.13 Gm.) thyroid daily improved; right index and thumb nails removed surgically and regrew normally; separation of others gradually returned to normal
26	W	F	46	Fracture of terminal phalanx; freezes; gains weight sleeps 9 hours; tires easily; previous B.M.R., —23	Separation of nail after fracture of finger	—19	2 grains (0.13 Gm.) thyroid daily and roentgen therapy; improved; recurred with typhoid fever; became normal on continued thyroid medication in 6 months
27	W	F	37	Freezes; sleeps excessively; easily fatigued	Onychauxis; irregular, thickened, dark buckled nails; early separation of nail of right index finger	—27	1½ grains (0.13 Gm.) thyroid daily for 5 months; nails normal; no recurrence in 2 years
28	W	F	34	Skin and hair dry; freezes; sleeps 8 to 9 hours; repeated miscarriages	Separation of finger and toe nails and other dystrophic changes for 4 years; eversion of nails of each little finger; space filled with hyperkeratotic material	—19	Fair improvement of separation; no change in dystrophies; has had recurrent separations; multiglandular dysfunction
29	W	F	24	Mild eczematoid dermatitis about finger tips	Nails of right thumb and index and middle fingers separated from formaldehyde solution (beauty parlor)	None	Dermatitis disappeared and nails improved on avoiding formaldehyde solution
30	W	F	21	Edema and eczematoid dermatitis of terminal phalanx of each finger; fingers remain moist with permanent wave fluid	All nails of both hands show ¼ to ½ separation	None	Wet dressing and ammoniated mercury ointment produced rapid improvement; condition recurs when same wave fluid is used

and dark, the teeth separated and the gums spongy. The basal metabolic rate was —47 per cent. She showed rapid improvement by prolonged treatment with thyroid extract.

Duemling [13] observed a white man aged 23 who had marked thickening of the palms and soles, general loss of hair and a basal metabolic rate of —13 per cent. He was otherwise well developed and in good health. His nails were ragged and split and covered only about half the nail bed. Duemling considered the changes typical of those noted in children with myxedema and cretinism and considered the case one of hypothyroidism. Barney [14] reported a case in which one toe nail became white and separated from the nail bed; when the nail regrew it was thick and yellowish. Later all nails of the fingers and toes became involved and were elevated from the nail bed, thin and brittle; the nail plates were uneven and showed longitudinal striation. The toe nails were thickened and elevated, and the space beneath was filled with horny masses. The Wassermann reaction was negative; scrapings and cultures for fungi gave negative results; the values for blood calcium and phosphorus were normal; the basal metabolic rate was —15 per cent. No improvement was noted from a high vitamin diet or from administration of thyroid.

Barrett,[15] in his report on the hereditary occurrence of hypothyroidism with dystrophic changes of the nails, presented the case of a patient with disorders of the hair and nails and abnormalities of the mental and nervous system. The scalp hair was scant and the eyebrows and the axillary and pubic hair reduced. The nails were short of the finger tips; the edges were thick and broken, with absence of the lunula. Histologic examination of the skin showed a myxedematous condition. The patient improved when given 5 grains (0.32 Gm.) of thyroid three times daily. The nails continued to grow; there were an increase of perspiration and an increased growth of hair of the scalp and eyebrows, and the exfoliation of the hands improved. The study of this patient's family of 61 members in six generations revealed that 14 of them had had abnormal changes of the nails and hair and varying types of mental change. Tobias [16] reported a similar case in which there were dystrophy of the nails and changes of the hair, and in the patient's family of 25

13. Duemling, W. W.: Dystrophy of the Hair and Nails; Keratodermia of the Palms and Soles; Hypothyroidism, Arch. Dermat. & Syph. **29**:163 (Jan.) 1934.

14. Barney, R. E.: Dystrophy of Nails, Arch. Dermat. & Syph. **31**:721 (May) 1935.

15. Barrett, A. M.: Hereditary Occurrence of Hypothyroidism with Dystrophies of the Nails, Arch. Neurol. & Psychiat. **2**:628 (Dec.) 1919.

16. Tobias, N.: Hereditary Familial Dystrophy of the Nails, J. A. M. A. **84**: 1568 (May 23) 1925.

persons covering four generations there were 12 with such dystrophic changes. Jacobsen [17] studied a family consisting of 64 members in five generations, 22 of whom had dystrophic changes in the nails and 18 of whom were hairless or had only scant downy hair. He stated that the cause was uncertain, but that certain of the physical changes in these persons are also seen in persons suffering from endocrine deficiency, notably hypothyroidism, and he concluded that there was considerable evidence to suggest that hypothyroidism may be directly inherited. Thompson [18] studied a similar family, of 65 members in four generations, 16 of whom had dystrophic changes of the nails; 11 were men and 5 were women. Some showed improvement when roentgen therapy was given, and they were later treated with thyroid medication. No report of follow-up observations was made.

Alderson [19] observed a white woman aged 49 with severe onychauxis involving all the finger nails and to less extent the toe nails. She improved rapidly on administration of thyroid, ½ grain (0.03 Gm.) three times daily for two weeks and then 1 grain (0.06 Gm.) three times daily for several months. The nails were considered normal at the end of nine months.

Behn and Besancon [20] reported the case of a boy aged 13 whose finger and toe nails became rough, thin and friable and who had a basal metabolic rate of — 17 per cent.

Rostenberg [21] presented a woman aged 37 who for ten years had abnormal nails; there were atrophic and dystrophic changes which involved more than a third of the nail. The nails were roughened, pitted and discolored. The Wassermann reaction was negative; the basal metabolic rate was + 48 per cent on one occasion and later was + 22 per cent. A similar case, in which there was associated hyperthyroidism, was described by Heller [9] in his monograph. Pardo-Castello [3] observed 2 cases of atrophy of finger and toe nails associated with hyperthyroidism. Shelmire [10] observed a patient with severe exophthalmic goiter who had separation of all the nails. Two months after partial thyroidectomy the nails were normal. Surgeons observing

17. Jacobsen, A. W.: Hereditary Dystrophy of the Hair and Nails, J. A. M. A. **90**:686 (March 3) 1928.

18. Thompson, H. B.: Hereditary Dystrophy of the Nails, J. A. M. A. **91**:1547 (Nov. 17) 1928.

19. Alderson, H. E.: Onychauxis and Thyroid Therapy, Arch. Dermat. & Syph. **5**:602 (May) 1922.

20. Behn, C. W., and Besancon, J. H.: Dystrophy of the Nails, Arch. Dermat. & Syph. **27**:359 (Feb.) 1933.

21. Rostenberg, A.: Anonychia and Onychatrophia Acquisita, Arch. Dermat. & Syph. **26**:581 (Sept.) 1932.

a large number of cases of hyperthyroidism say that they frequently see separation of the nails and consider this condition one of the symptoms of hyperthyroidism.

In an analysis of 150 cases of myxedema, Hun and Prudden [22] found changes of the nails in 75 per cent. Howard found abnormal nails in 86 per cent and changes in the hair in 93 per cent of his patients with myxedema.

Hollander and Fisher [23] observed a patient whose finger and toe nails were opaque, with dark brown discolored areas. The lunulae were absent, and the case was considered one of hypopituitarism. Guy, in discussing the case, stated that he had observed a similar condition due to hypothyroidism.

Hollander [24] reported a case of onychauxis due to hypopituitarism. The patient was a white boy aged 9 years who had dry, rough, brownish, grooved and transversely striated nails of both the hands and the feet. Dryness of the skin and hair had developed gradually, with absence of axillary and pubic hair, small genitalia and feminine characteristics. Hollander also described 2 cases of dystrophia adiposogenitalis [25] with changes of the hair and nails, small genitalia and obesity. He considered the cutaneous and ungual changes a result of the glandular dysfunction.

Combes [26] observed a boy aged 12 years who presented dystrophic changes of the nails and keratoses of the palms associated with Fröhlich's syndrome. The nails were hypertrophic, opaque, ridged and brittle. The toe nails were similar and presented severe onychogryposis. The basal metabolic rate was — 21 per cent.

Lisser [27] observed a eunuchoid who had suffered a testicular injury eleven years previously. The nails of the fingers and toes were dry, brittle and increased in thickness. Implantation of testicular substance produced great general improvement, and the nails became normal. Lisser stated that trophic disturbances of the skin, hair, nails and teeth are common in deficiency diseases of the glands of internal secretion, particularly hypothyroidism, hypopituitarism and hypogonadism.

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22. Hun, H., and Prudden, T. M.: Myxodema, Am. J. M. Sc. **96**:1 (July) 1888; cited by Barrett.[15]

23. Hollander, L., and Fisher, J. W.: Onychauxis, Arch. Dermat. & Syph. **30**: 453 (Sept.) 1934.

24. Hollander, L.: Onychauxis Due to Hypopituitarism, Arch. Dermat. & Syph. **2**:35 (July) 1920.

25. Hollander, L.: Pituitary Gland Dystrophies, Arch. Dermat. & Syph. **7**: 632 (May) 1923.

26. Combes, F. C.: Onychauxis and Keratosis Palmaris, Arch. Dermat. & Syph. **24**:711 (Oct.) 1931.

27. Lisser, H.: Onychauxis in a Eunuchoid, Arch. Dermat. & Syph. **10**:180 (Aug.) 1924.

Pende [28] observed fragile, thin nails with striae, white spots, atrophy and slow growth with similar changes of the hair in hypoplastic conditions, particularly hypothyroidism. In hypopituitarism the lunula is small or absent. Hypogonadism produces thin nails. In hyperthyroidism and hyperpituitarism there are well developed, shiny nails that grow rapidly. Meakins [29] stated the belief that low metabolism is observed in diseases due to deficient function of the pituitary, adrenal and gonad glands without symptoms of myxedema. The adrenal gland raises metabolism through the effect of epinephrine on cells and by its influence on the thyroid.

White [30] has reported 7 cases of changes in the nails which were considered due to avitaminosis; in 2 of these cases there were lowered basal metabolic rates. They did not improve on administration of thyroid, but high doses of vitamins B_2 and D produced rapid improvement. Pardo-Castello [3] stated that he has seen no cases of changes in the nails proved due to vitamins. Clinical experimentation [31] seems to indicate that the administration of vitamin A by mouth may produce cutaneous effects similar to those sometimes seen after administration of thyroid preparations. This is seen especially in cases of "dry skin," brittleness of the nails and follicular keratoses and in some cases of keratotic palms and soles and in mild ichthyosis and erythroderma. Goldsmith [32] in a discussion of vitamins stated that vitamins A and B_1 are antagonistic to thyroxin, vitamin C deficiencies cause a diminished production of epinephrine while vitamin D is synergistic with parathyroid, especially in tetany. Vitamins may have an indirect endocrine effect or function.[33]

Anderson [34] recently reported a case of spoon nails, dysphagia and cheilitis in a woman suffering from severe anemia. In his conclusion he stated that the ungual changes were possibly due to mild hypothyroidism, which is frequently associated with severe anemia.

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28. Pende, N.: Constitutional Inadequacies: An Introduction to the Study of Abnormal Constitutions, translated by S. Naccarati, Philadelphia, Lea & Febiger, 1928, p. 140.

29. Meakins, J. C.: The Practice of Medicine, ed. 2, St. Louis, C. V. Mosby Company, 1938, p. 883.

30. White, C.: Onychia Due to Chronic Hypovitaminosis, J. A. M. A. **102**:2178 (June 30) 1934.

31. Wise, F., and Sulzberger, M. B.: The Year Book of Dermatology and Syphilology, Chicago, The Year Book Publishers, Inc., 1938, p. 6.

32. Goldsmith, W. N.: Recent Advances in Dermatology, Philadelphia, P. Blakiston's Son & Co., 1936, p. 485.

33. Cowgill, G. R.: The Vitamin B Requirements of Man, New Haven, Conn., Yale University Press, 1934.

34. Anderson, N. P.: Syndrome of Spoon Nails, Anemia, Cheilitis and Dysphagia, Arch. Dermat. & Syph. **37**:816 (May) 1938.

CONCLUSIONS

1. Cases of onycholysis associated with reduction in the basal metabolic rate are reported. Improvement followed thyroid medication in the majority of the cases.

2. Considerable evidence is presented that there is a relation between diseases of the nails and endocrine dysfunctions.

3. The influence of the hormones on the development of the skin and its appendages in both physiologic and pathologic processes should receive more consideration from the dermatologist.

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ABSTRACT OF DISCUSSION

DR. V. PARDO-CASTELLO, Habana, Cuba: Dr. Fox has done well in calling attention to the cause of these dystrophies of the nails. He has been unusually fortunate to gather such a large number of cases of onycholysis and to prove in the majority of them an etiologic connection with hypothyroidism, as shown by the low basal metabolic rate and by the excellent results of the specific treatment.

However, onycholysis is not always due to hypothyroidism. I believe that it may be due to a host of different causes, among which thyroid dysfunction seems to be a frequent one.

I agree with Dr. Fox that aside from the infectious, traumatic, parasitic and symptomatic diseases of the nails coincident with diverse dermatoses, the conditions of the nails produced by endocrine disturbances are the most common. This report shows how a disturbance of the nail growth may be the first, and for the time being the only, apparent symptom of endocrine imbalance. I think that physicians in general do not pay enough attention to the minor changes of the nails, which may yet be of importance in arriving at a satisfactory diagnosis in many cutaneous, as well as other, diseases.

DR. J. GARDNER HOPKINS, New York: I am grateful to Dr. Fox for this presentation because some light on disorders of the nails is certainly needed. I should like to ask Dr. Fox whether he has seen any spoon nails. I have seen several cases in which the patient had the same type of basal metabolic rate he reports in the low range of normal and in which the condition of the nails improved after medication with thyroid extract. Another point of great interest to me is that the table of basal metabolic rates, if I made it correctly, shows many rates from — 12 to — 14. Such rates are usually regarded as normal. I am sure, however, that in certain cutaneous diseases rates in the lower range of normal have to be regarded as significant.

DR. SAMUEL AYRES JR., Los Angeles: I should like to ask Dr. Fox if he made any observations on the condition of the toe nails of these patients in correlation with the finger nails. I thought possibly that there might be some significance in the fact that so many of these patients are females. That also calls up the question of nail polish and polish removers containing acetone and other ingredients having affected the nail. I have encountered many women showing separation of the nails or transverse splitting, which I have always regarded as possibly due to nail polish or polish remover. I wonder whether the separation from the nail bed in some of Dr. Fox's cases might not be of the same nature.

DR. S. WILLIAM BECKER, Chicago: Dr. Fox asked me to discuss this paper, since I have made a study, as yet unpublished, of certain diseases of the nails which included a rather large percentage of cases of onycholysis. The study was inspired

by a patient with severe onychia of the type called by Heller "onychogryphosis due to eczema" and described in the *Archiv für Dermatologie und Syphilis* (**163**:337, 1931). My patient was 30 years of age and had had the condition for eight months. All of the nails of the right hand and the first two of the left hand were involved in a severe overgrowth and were yellow and crumbly. In addition to the changes in the nails, the involved fingers of both hands showed chronic exudative dermatitis without definite vesiculation. Repeated search for fungi by both the potassium hydroxide method and culture was fruitless. Capillary studies of the folds of the nails which were yet uninvolved showed vasodilatation. The patient was presented before the Chicago Dermatological Society (ARCH. DERMAT. & SYPH. **24**:698 [Oct.] 1931), where the consensus was in favor of a fungous origin. Further search was made by potassium hydroxide preparations and culture, with negative results. Portions of the nail were removed, sectioned and studied microscopically, but no fungi were found. When even a small amount of nail had been removed, pain was experienced and bleeding was evident. There was therefore extensive overgrowth of the nail bed itself. On section, blood vessels and collections of nucleated cells were seen, but no fungi.

Since fungi could not be found, it was decided to treat the patient as though only the dermatitis were present, which was diagnosed exudative neurodermatitis. The dermatitis cleared up immediately, and the nails became normal just as soon as new nails could grow. Some three years later juxta-articular nodules developed due to syphilis, which had been contracted in the meantime. The patient was again presented before the Chicago Dermatological Society (ARCH. DERMAT. & SYPH. **31**:744 [May] 1935), at which time the diagnosis was confirmed and the nails were normal.

In contrast to this severe type of onychia, other patients with exudative neurodermatitis show milder changes of the type usually called "eczema of the nails." Patients with the dry type of neurodermatitis (flexural, atopic eczema), on the other hand, show a type of onychia which falls in the classification of onycholysis, which is the subject of Dr. Fox's paper. I found that treatment of the neurodermatitis caused the lesions of the nail to improve, so that in case there is no mechanical reason for the onycholysis, as reported by Templeton, I make a diagnosis of neuro-onychia, treat the patient accordingly and obtain good results. I was much pleased to hear Dr. Fox link the changes in the nails with the disturbance of the endocrine system. I prefer to call the condition neuronychia, but, after all, I know that the sympathetic nervous system and the endocrine glands are inseparable functionally. Dr. Fox found onycholysis much more frequently in women. My studies have shown that functional disease is more frequent in women than in men, but not to so great a degree. The question of medication with thyroid has always intrigued me. When Dr. Russell Wilder of the Mayo Clinic was chairman of the department of medicine at the University of Chicago, I discussed with him the reason for the low basal metabolic rate in patients with functional disease. He did not know the exact cause but was inclined to doubt that it was due entirely to thyroid dysfunction. I have never tried medication with thyroid myself, but have had patients who had received it elsewhere, usually with disappointing results. It is gratifying to hear of Dr. Fox's excellent results. I should like to ask him whether capillary studies at the nail fold have been made in his cases, especially in normal nails, and whether any of his patients had other dermatoses.

DR. HIRAM E. MILLER, San Francisco: I should also like to ask Dr. Fox how he explains the high incidence of women—28 women to 2 men. It has occurred to me that while the basic cause may be metabolic, the exciting factor probably is nail polish, acetone and similar preparations.

DR. LOUIS A. BRUNSTING, Rochester, Minn.: I should like to ask Dr. Fox whether he has observed cases of frank myxedema in association with onycholysis. It should be recognized that reports of the basal metabolic rates, especially single readings, may be subject to a considerable percentage of error. Readings are of less importance generally in hypothyroidism than in hyperthyroidism. In cases of extensive involvement of the skin by exfoliative dermatitis, the basal metabolic rate is elevated often to 50 per cent above normal without evidence of hyperthyroidism. In these cases there is an alteration from normal in the radiation of body heat, and the basic formula for recording the rate by the measurement of the exchange of oxygen and carbon dioxide through the lungs does not obtain. The administration of thyroid extract in cases in which there is a lowered basal metabolic rate is usually well controlled, but a word of warning may be in order in the use of such treatment in the goiter belts and in the management particularly of older persons who may have an adenoma of the thyroid.

DR. EVERETT C. FOX, Dallas, Texas: In answer to Dr. Brunsting's question regarding the basal metabolic rates, I have found low basal metabolic rates in many of these patients, as noted in the table, but I have not found any patients with clinical myxedema. I believe that one can determine more from the clinical history and physical examination regarding thyroid deficiency than by the basal metabolic rate, particularly as it is usually done, by the patient's going to the laboratory on the morning of the test. It is more accurate when the patient is hospitalized over night, and some patients have shown lower rates when checked that way. The dose of thyroid extract has been kept low because of what Dr. Brunsting mentioned. In no case has the dose been raised above 3 grains (0.195 Gm.) daily. When I have to give more than that, the patient is turned over to an internist or an endocrinologist. Regarding nail polish, most of my patients have been told at the beauty parlor that this is the cause of their trouble and as a result have left off nail polish for months. This factor certainly has to be considered as well as other irritants. Disturbances of the nails from chemical irritants, such as a solution of formaldehyde and permanent wave fluid, were reported in beauty parlor operators. Several patients had involvement of the toe nails, but certainly not as frequently as of the finger nails. I do not know why the series should be as high in women except for the explanation offered by Dr. Becker of nervous and vascular instability. I think that in some of these cases there is probably more chance for vascular disturbance than in others. Certainly a low basal metabolic rate may be observed in many of them. In some cases dyshidrosis has been classified as a neurovascular disturbance, and low basal metabolic rates have been present. Capillary studies have not been made. Many of the patients would probably have capillary changes associated with the changes of metabolism and the growth and cornification of the nails. There are a number of reports in the literature on spoon nails, some of which have improved on medication with thyroid. In many cases the condition of the nails has been associated with anemia. Almost invariably, severe anemia is associated with hypothyroidism. The changes in the nails probably occur as a result of hypothyroidism associated with severe anemia. I appreciated Dr. Pardo-Castello's discussion. Certainly this method of treatment will not cure onycholysis in all cases. Hypothyroidism is only one etiologic factor of a large group which includes pyogenic and fungous infections and changes associated with the inflammatory dermatoses as well as endocrine dysfunctions. The condition may also be related to trauma. In this particular group that I am reporting, I believe that under the method of treatment used the patients have shown more improvement and have remained well longer than those treated by any other means previously used.

URINARY EXCRETION OF INDOXYL (AS INDICAN) BY INFANTS WITH ECZEMA

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MARGARET M. KLUMPP, M.D., COLLABORATOR
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Interest in the metabolism of a compound essentially toxic and regularly formed in the enteric canal will continue, at least until a complete clarification of the mode of its detoxication is established. Furthermore, the toxicity of the compound will continue to justify studies directed toward disclosing the relation between it and disease processes. I have reference to the substance indole. This heterocyclic nitrogenous compound, a degradation product of the amino acid tryptophan, has as yet achieved no clinical significance beyond its traditional indictment of complicity in the production of so-called autointoxication or biliousness. This relation has the laboratory background of an increased excretion of indican in the urine, determined by crude qualitative tests.

The introduction of newer and more accurate analytic methods in biochemistry not alone supplies instrumentalities for the elucidation of physiologic and clinical problems but serves as inspiration for the testing of theories in physiology and pathogenesis. Furthermore, the newer analytic methods in measurement of the indoxyl derivatives of indole have sponsored the continued interest in the metabolism of indole. My interest in the problem dates from my development of quantitative analytic methods for the estimation of indoxyl compounds in urine and blood.

By these methods the following data have been established: (1) the normal concentration of indoxyl in blood;[1] (2) the daily excretion of it in urine[2] as indican in amounts far in excess (75 to 150 mg.) of what had until then been considered within the normal range, and (lately) (3) the excretion in the newborn of indican in amounts com-

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Read at the Sixty-Second Annual Meeting of the American Dermatological Association, Inc., Monte-Bello, Quebec, Canada, June 3, 1939.

1. Sharlit, H.: A Method for the Quantitative Estimation of Indoxyl Compounds in Blood, J. Biol. Chem. **104**:115, 1934; The Concentration of Indoxyl Compounds (Indican) in Blood, J. Lab. & Clin. Med. **20**:850, 1935.

2. Sharlit, H.: A Method for the Quantitative Estimation of Indoxyl Compounds in Urine, J. Biol. Chem. **99**:537, 1933.

parable in terms of relative body weight to that excreted by adults.[3] It was this last finding that supplied the background for the study herein reported and the base line from which to interpret the findings.

The several features of indole metabolism definitely established are these:

1. Indole is wholly of exogenous origin (formed in the intestines from tryptophan.

2. One way of detoxicating it is through oxidation to indoxyl and conjugation with sulfuric acid to form indican (potassium indoxyl sulfate). This is accomplished by the liver.

3. Indican is harmless and readily excreted by the kidneys.

4. The administration of indole orally or parenterally[4] increases indican excretion in an amount to account for but 50 per cent of the exhibited indole.

5. The route or routes of passage of the other 50 per cent of indole are still unknown, and the possibility that these routes represent failure to detoxicate effectively poses the danger of indole to the integral organism.

6. The excretion of large amounts of indican in the urine may be accepted as evidence of inordinate putrefaction of protein in the intestine.

Single chance samples of urine were collected from each of 35 infants between the ages approximately of 2 months and 2 years, each of whom had an eruption and most of whom had some form of eczema. The specific gravity of each sample (except a few in which the total volume was too small for an acceptable reading) was carefully taken and a quantitative determination made for indican. The specific gravity is a substantially adequate index of the concentration of the solids in urine and may properly serve to indicate, with respect to a given dissolved constituent, the importance of the general concentration of the dissolved solids in the sample examined. This rapid check on the significance of excretion in chance samples, when the chief concern is knowledge of the absolute amount excreted on a twenty-four hour basis, is the only one available when the collection of twenty-four hour excretions is well nigh impossible, as was the case with these nonhospitalized infants.

For this reason the results of the analyses given in the table are listed in an order determined by the specific gravity of the several

3. Sharlit, H.: Indican Excretion in the New-Born, Arch. Pediat. **55:** 277, 1938.

4. Sharlit, H.: Unpublished data. Similar findings have been published by others.

samples. Therein will be noted a definite correlation between indican concentration and specific gravity—evidence of the anticipated reliability of the specific gravity in marking the influence of the general density of the sample on the concentration of indican found. This was also found in the samples from healthy newborn infants, though with those the total nitrogen was used as an index to the measure of concentration of the solids. On the whole, it must be said that these data gave definite evidence of an indican excretion in these infants in excess of

Results of Analyses of Urine (Cases Listed in Order of Ascending Values of Specific Gravity of Samples Examined)

Case No.	Age	Diagnosis	Specific Gravity of Urine	Indican, Mg. per Liter
1	2 yrs.	Dermatitis venenata	1.007	Faint trace
2	20 mos.	Infantile eczema	1.007	Trace
3	4 mos.	Infantile eczema	1.010	Faint trace
4	7 mos.	Atopic eczema	1.013	Trace
5	2 mos.	Infantile eczema	1.013	25
6	1 yr.	Atopic eczema	1.014	16
7	1 yr.	Atopic eczema	1.016	Trace
8	4 mos.	Infantile eczema	1.017	Trace
9	1 yr.	Infantile eczema	1.018	Trace
10	2 yrs.	Infantile eczema	1.018	47
11	17 mos.	Atopic eczema	1.019	40
12	2 yrs.	Impetigo; dermatitis venenata	1.020	17
13	2 yrs.	Infantile eczema	1.020	39
14	2 yrs.	Urticaria	1.021	27
15	14 mos.	Infantile eczema	1.024	32
16	2 yrs.	Neurodermatitis	1.024	18
17	5 mos.	Infantile eczema	1.025	Trace
18	2 yrs.	Infantile eczema	1.026	44
19	2 yrs.	Infantile eczema	1.026	30
20	2 mos.	Infantile eczema	1.026	29
21	2 yrs.	Dermatitis venenata	1.027	84
22	2 yrs.	Pyoderma	1.027	35
23	2 yrs.	Urticaria	1.028	47
24	2 yrs.	Infantile eczema	1.030	17
25	15 mos.	Atopic eczema	1.031	54
26	1 yr.	Herpes simplex	1.031	80
27	10 wks.	Seborrheic eczema	1.032	84
28	2½ yrs.	Atopic eczema	1.033	62
29	21 mos.	Infantile eczema	1.033	80
30	2 yrs.	Infantile eczema	1.034	67
31	1 yr.	Atopic eczema	?	Trace
32	2 yrs.	Infantile eczema	?	38
33	2 yrs.	Neurodermatitis	?	78
34	2 yrs.	Infantile eczema	?	87
35	16 mos.	Infantile eczema	?	59

what might have been expected on a basis of my reported findings in the healthy newborn, though distinctly less than might have been anticipated in the presence of protein putrefaction.

To the extent that this is an exposure of the true state of affairs it may be concluded that eczema in infants is not usually associated with enteric protein putrefaction. I believe that conclusion to be in general harmony with clinical opinion and experience with eczema of infants; however, this statement must be read in the light of the influence of intestinal stasis and its definite relation to indican production.

Costiveness regularly increases indicanuria, and an intestinal purge may be relied on to reduce it precipitately. Constipation is a complaint so common that physicians have almost come to ignore it as a contributing factor to disability, yet those who make a fetish of combating it as the first approach in the relief of none too obviously explained symptoms have on countless occasions reported astonishing success. How important constipation is in the practice of dermatology is impossible to judge. Certainly reported studies pertaining thereto are exceedingly few. Still, constipation as a possible factor in the production or the maintenance of eczema in infants is seriously considered. Goodman and Burr [5] in the histories of 206 cases of infantile eczema reported constipation present in 85 per cent. Strickler, Fisher and Lowenburg [6] studied the gastrointestinal motility by roentgen examination of the tract in 33 children with the eczema of infants and found intestinal stasis in more than half of them. Of course, the pediatric approach to the therapy of eczema in infants regularly stresses the necessary attention to accompanying constipation or diarrhea. My data may be said to corroborate these reported findings of constipation in infants with eczema.

Sagers,[7] of the medical corps of the United States Navy, recently made a short report in the service medical bulletin, which, strangely enough, he called "Allergy, Autointoxication and Indicanuria." In a group of service men with varying, etiologically elusive complaints (including 1 with eczema) he followed the plan of recording the degree of indicanuria in several samples from each patient each day and correlating these findings with the nature of the diet in terms of specific articles of food. By elimination and substitution of articles of diet, he sought for each patient a list of foodstuffs that led to a minimum indicanuria. On diets so determined his patients reported much relief. Incidentally, the patient with eczema was cured. I mention without comment his theory that irritation of the intestinal mucosa may influence the selective absorptions through that lining and admit to the circulation toxins and the elements necessary to invoke symptoms and, I presume, to assist in setting up the allergic mechanism.

My findings, too, may be said to support in a negative way the concept of an allergic background in most of these infants with eczema. While the production of indican is a hepatic function, too little is known

5. Goodman, H., and Burr, M. E.: Eczema in Infancy and Childhood, Arch. Pediat. **54**:30, 1937.

6. Strickler, A.; Fisher, M. K., and Lowenburg, H.: A Probable Etiological Factor in Infantile Eczema Based on X-Ray Examinations of the Gastro-Intestinal Tract, Arch. Pediat. **53**:397, 1936.

7. Sagers, J. K.: Allergy, Autointoxication and Indicanuria, U. S. Nav. M. Bull. **34**:67, 1936.

of the complete story of indole metabolism to justify a discussion of this function on the basis of only this type of investigation. Speaking generally of the problem of intestinal putrefaction, it may be pointed out that indican production may serve as a reliable measure of its existence as directly applicable to protein digestion. In this connection, attention may be called to the possible usefulness of this type of investigation as correlative to studies in porphyrin production. The seemingly confused findings resulting from the quantitative studies on porphyrin elaboration in cases of suspected photosensitive dermatoses may receive clarification if such studies receive accompanying estimations of indican production as a measure of the putrefactive background for the various porphyrin body formations.

To probe by sampling the probable fertility of a way of study in the elucidation of disease processes can never in itself give completely meaningful findings. When the attempt results in a dry bore, publication of the experiment seems justified only if the procedure per se has genuine physiologic meaning. For then publication calls attention to a helpful way of study of other and possibly more appropriate problems. I believe this to be true with respect to the study of indole metabolism.

One need make no plea in these times for routine urinalysis in dermatologic practice. Quantitative indican measurements can be routinely secured with ease, and it is not beyond expectation that through such routine recordings evidences or clues may be revealed when even ingenious casting here and there might fail to produce a "haul."

SUMMARY

The quantitative estimation of indican on chance samples of urine in 35 cases of infantile dermatoses, chiefly eczema, showed definitely increased excretions, probably due to intestinal stasis.

ABSTRACT OF DISCUSSION

DR. MARION B. SULZBERGER, New York: I am not competent to discuss Dr. Sharlit and Dr. Klumpp's paper from the chemical or the biochemical point of view, but I think one can take it for granted that they have demonstrated a quantitative difference between normal infants and infants with infantile eczema in regard to a certain component of the urine. They explain this difference on the basis of the probable existence of constipation in infants with eczema as contrasted to infants without eczema. In my material, most eczematous eruptions in infants are not seborrheic or contact type dermatitis but atopic dermatitis. There is now a rather long list of observations on the obvious alterations in atopic persons as contrasted to normal persons. For example, one can say that atopic persons are inclined to have vasomotor instability, including vagotonia; that many seem to have slightly more than the normal tolerance for sugar; that many have white dermographism, and now, perhaps, that they are inclined to spasm and to spastic constipation. The question is: What may one conclude from the finding of these abnormalities? At present, I believe one can conclude only that the abnormali-

is, in all probability, related in some way to the atopic condition. It may be the result of the atopic constitution or the result of the presence of atopic disease—in this instance, a cutaneous manifestation of atopy. In other words, here the cutaneous disease may be in some way attributable to the constipation, or the constipation may be in some way due to the cutaneous disease or both may be the result of some third factor. It seems to me that it is today quite obvious that the existence of disease often depends on a chain of many links, and the breaking of only one of these links may be sufficient to interrupt the chain of factors operative in the causation of the disease. That explains why in some cases atopic disease may respond to combating of the constipation, in others to correcting the sugar tolerance, in others to sedatives, in others, to rest, to change of environment, to reducing the exposure to atopens, and in some even to relieving nervous tension or psychic stresses. It is probable that in each instance therapy has simply attacked one of the factors and has broken one link in the chain on which the existence of disease depended.

Dr. Herman Shaplit, New York: I think there is a practical implication in the use of estimations of indican in the control of constipation. Many disease processes are complicated by it. The fact that one knows about a physiologic factor (constipation) which never operates in favor of the patient but usually against him is good reason to feel that it is good practice to attempt to clear it up. In dealing with eczema or atopic dermatitis, one is invariably impressed with the idea that diet may have something to do with it. In approaching this dietary phase, rather than attempt elimination and substitution of special foodstuffs helter skelter, one would do better to direct such changes under the guidance of a test on urine, such as for indican. Aiming to bring indicanuria to a minimum may be an effective approach to the dietary phase of the treatment of eczema. The technic of estimation may be readily adapted to office practice.

Clinical Notes

GENERALIZED EXFOLIATIVE PSORIASIS AND MYCOSIS FUNGOIDES

IRVING L. SCHONBERG, M.D., CLEVELAND

Keil,[1] in an extensive study of parapsoriasis en plaques disséminées and incipient mycosis fungoides, suggested that the former dermatosis probably is the precursor of the latter in most, if not all, cases. Wise and Sulzberger,[2] commenting on this observation, stated the belief that the incidence of mycosis fungoides would be much greater in a given community if this were true. They have, however, observed some cases of parapsoriasis en plaques in which there finally appeared, after years, clinical as well as microscopic evidence of mycosis fungoides. Fox,[3] in 1913 reported a case of mycosis fungoides following psoriasis.

The case to be described here is deemed worthy of report since long-standing psoriasis was followed by mycosis fungoides.

REPORT OF A CASE

Past History.—J. S., a Jew 45 years of age, had, except for a dermatosis, enjoyed good health. The eruption started thirty-four years before I saw him, as "red spots" over his entire body. These spots soon acquired a scaly character and finally coalesced, forming large scaly red plaques. During the past year he had noticed red rings and patches which appeared different from the original lesions. During the past thirty years he had noticed improvement during the warm weather, but during the last summer the areas had seemed more persistent. Until the last year there had been no subjective symptoms. During the past few months itching had been a notable feature, especially over the chest and abdomen.

Present Illness.—When first observed, on Feb. 13, 1939, the patient presented a diffuse erythematosquamous process involving the scalp, face, trunk and extremities. On the scalp there was a "piling up" of silvery scales. The ears and upper eyelids and brows shared in the erythematous scaly process. On the trunk there were large areas, varying in size from that of a silver dollar to that of a palm, noninfiltrated, red, sharply demarcated and covered with loosely adherent scales. There were similar but smaller areas on the extremities. In addition to the scaly lesions, the trunk, back and thighs presented red and brownish red nummular plaques varying in size from that of a quarter to that of a palm,

1. Keil, H.: Parapsoriasis en Plaques Disséminées and Incipient Mycosis Fungoides: A Critical Review with a Report of an Illustrative Case, Arch. Dermat. & Syph. **37**:465 (March) 1938; Parapsoriasis en Plaques Disséminées and Incipient Mycosis Fungoides: Supplementary Data on Their Relationship, ibid. **38**:545 (Oct.) 1938.

2. Wise, F., and Sulzberger, M. B.: Year Book of Dermatology and Syphilology for 1938, Chicago, The Year Book Publishers, Inc., 1938.

3. Fox, H.: Mycosis Fungoides Following Psoriasis, J. A. M. A. **61**:330 (Aug. 2) 1913.

definitely infiltrated and unquestionably distinct from the surrounding scaly skin. The borders were sharply defined and appeared to be slightly raised. Some of the lesions were annular in appearance. The ringlike infiltrations enclosed small scaly islands. The skin markings on the infiltrated areas were exaggerated. There were numerous crusted linear areas on the trunk and shoulders. On the lower extremities were several lima-bean-sized ulcerated areas accompanying varicose eczema.

The results of serologic examination of the blood and the blood count were normal. Histologic examination (by Drs. David L. Satenstein and Wilburt Sachs) was made of a section from a lesion on the chest.

Microscopic Description.—Throughout the entire upper and middle portions of the cutis was an intense cellular infiltrate. It was composed of small round wandering connective tissue cells, plasma cells and histiocytes. Throughout this infiltrate in some areas a fine reticulum was present. There were some breaking up of the cellular elements and some grouping of the cells. In the upper part of the cutis there was a moderate amount of edema and leukocytes. The epidermis was irregularly acanthotic and in some small areas parakeratotic. In the other zones the granular layer was retarded. No cell nests were present in the epidermis. The microscopic diagnosis was mycosis fungoides.

SUMMARY

A case of mycosis fungoides is presented. This condition followed a long-standing generalized psoriasis, of thirty-four years' duration. Pruritus, which was absent for thirty-four years, developed after the appearance of the infiltrated plaques of mycosis fungoides.

524 Keith Building.

HISTOLOGIC STUDY OF THE FREI REACTION PAPULE

LESLIE M. SMITH, M.D., EL PASO, TEXAS

The indolent character and the unusual persistence of the Frei test papule prompted its microscopic study at several stages of its evolution. Three patients with proved lymphogranuloma venereum were given injections of 0.1 cc. of Frei antigen intracutaneously in the arm. Positive reactions developed in all, and no reactions were obtained in other persons who were used as controls. A papule was removed from one patient at the end of twenty-four hours, from another at seventy-two hours and from a third five days after the test was performed. These specimens were prepared according to routine and stained with hematoxylin and eosin.

APPEARANCE AT VARIOUS STAGES

Reaction at Twenty-Four Hour Stage.—The epidermis showed marked intercellular and intracellular edema. Many of the cells were vacuolated, and in places there was some spongiosis, approaching vesicle formation. In the cutis there was moderate edema, and accumulations of lymphocytes and a few polymorphonuclear leukocytes were seen in perivascular spaces in the upper and middle strata.

Reaction at Seventy-Two Hour Stage.—There were slight hyperkeratosis and some edema in the epidermis, though less edema than at the twenty-four hour stage. In the cutis light edema and a noticeable increase in connective tissue cells were apparent. In the perivascular spaces throughout the cutis and about the sebaceous and sweat glands there was a decided infiltration composed of lymphocytes. One sebaceous gland showed degenerative changes apparently due to the pressure of the infiltrate.

Reaction at Five Day Stage.—The appearance differed little from that at the seventy-two hour stage. The epidermis showed less edema and no spongiosis. The infiltrate in the cutis was composed of lymphocytes which were massed about the vessels and superficial and deep parts of the appendages. Connective tissue cells were rather markedly increased.

COMMENT

The histologic picture of the Frei reaction is, then, as follows: Soon after the injection there is edema in the epidermis, with the production of spongiosis and histologic vesicles. It is easy to see how such a reaction might proceed to the formation of a clinical vesicle. After seventy-two hours this superficial edematous process subsides, and the cellular infiltrate in the cutis becomes more marked and is grouped around the blood vessels and appendages. Whereas early in the process the infiltrate is composed of lymphocytes and polymorphonuclear leukocytes, in the later stages it becomes practically a pure lymphocytic infiltrate with a decided increase in connective tissue cells. The rather dense character of the cellular infiltrate, extending fairly deep into the cutis, and the increase in connective tissue cells would seem to explain the indurated character and the persistence of the papule.

SUMMARY

A histologic study of Frei reaction papules at three stages of their evolution is presented, with the idea of correlating the clinical appearance of the papule and its histologic structure.

931 First National Bank Building.

Minor Notes

SENSITIVITY TO GENTIAN VIOLET (METHYLROSANILINE)

MARVIN B. GOLDSTEIN, M.D., YOUNGSTOWN, OHIO

Mrs. L. W., a white woman aged 45, was first seen in September 1939, complaining of severe pruritus vulvae. A diagnosis was made clinically and microscopically of monilial infection. A 3 per cent aqueous solution of gentian violet (methylrosaniline) was prescribed. The monilial infection began to clear up, but wherever the solution came in contact with the skin pustular dermatitis developed. At one time a drop was spilled on the thigh, and the dermatitis developed on the site. A patch test was done on the arm, with a positive result. The patient was presented at the Pittsburgh Dermatological Society [1] while the dermatitis was still present.

The application of gentian violet was discontinued, and the dermatitis cleared up. Then the remaining monilial infection was treated with a 3 per cent solution of cresyl violet, with good results. The patient showed no sensitivity to the cresyl violet.

1. Goldstein, M. B.: Arch. Dermat. & Syph., to be published.

Obituaries

JOSEPH LEE KIRBY-SMITH, M.D.
1882–1939

Joseph Lee Kirby-Smith, a pioneer dermatologist in the South, was born in Sewanee, Tenn., in 1882. He was educated at the Sewanee Military Academy and at the University of the South Medical Department, graduating in 1906 from the latter institution with a degree of Doctor of Medicine and with highest honors. From 1906 to 1910 he did graduate work in dermatology in New York, including practice in services at Bellevue Hospital and at the New York City Department of Health hospitals, and served for eighteen months as a member of the house staff of the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital. He also served as instructor of dermatology at New York University, at the Bellevue Hospital Clinic and at Dr. Fordyce's clinic.

He entered the practice of dermatology in Jacksonville, Fla., in 1911 and was active in practice until his death. For many years he served as chief of the department of dermatology at St. Vincent's, St. Luke's and Duval County hospitals and was dermatologist to the Riverside Hospital.

The Section on Dermatology and Syphilology of the Southern Medical Association, the Southeastern Dermatological Association and the Florida Society of Dermatology and Syphilology, of all of which he was a member, owe much to his genius for organization. He was also a diplomate of the American Board of Dermatology and Syphilology, a member of the American Medical Association, the American Society of Tropical Medicine and the American Society of Parasitology and a fellow of the American Academy of Dermatology and Syphilology.

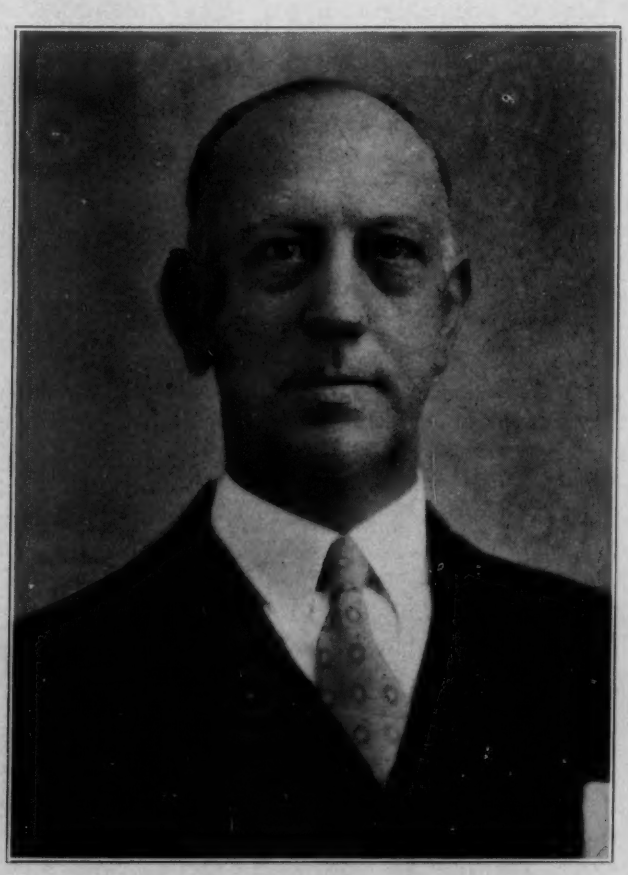
He was born of fighting stock. His father was the confederate general Edmund Kirby-Smith, commander of the department of the Southwest during the Civil War. Though handicapped by deafness as a result of an accident while playing football, Dr. Kirby-Smith, like his illustrious father, never surrendered or asked quarter because of the odds against him but used his sharpened powers of observation and his keen analytic mind to nullify a physical handicap. Because of this handicap, it was in a clinic that Kirby-Smith was at his best, his remarks being always pointed and without equivocation.

He was remarkably resourceful and dextrous in cutaneous therapeutics, and his sincere and abiding interest in the welfare of his patients engendered their faith and confidence in him. With his striking, aggressive, jovial personality, he seemed tireless and for many years conducted one of the largest dermatologic practices in the country.

Kirby-Smith contributed numerous articles to the literature but is best known for his studies on Agamonematodum migrans as a cause

of "creeping eruption." This work gained recognition abroad, and he discussed the subject before the London Medical Association in 1936. He was later awarded the degree of Doctor of Science by his Alma Mater for his research.

His social activities included membership in the Phi Delta Theta fraternity, Florida Yacht Club and Sons of the American Revolution.



JOSEPH LEE KIRBY-SMITH, M.D.
1882-1939

He was a member of the Church of the Good Shepherd. During the World War he served as a First Lieutenant in the Medical Corps, and after the war he was appointed a consultant in the United States Public Health Service.

Dr. Kirby-Smith died in Jacksonville on Nov. 5, 1939, after an illness of several months. He is survived by a widow and three daughters.

ELMO D. FRENCH, M.D.

Abstracts from Current Literature

EDITED BY DR. HERBERT RATTNER

ECZEMA AND ITS PRACTICAL MANAGEMENT. F. WISE and J. WOLF, J. A. M. A. **111**:2106 (Dec. 3) 1938.

Wise and Wolf enumerate the factors thought to be primarily and secondarily responsible for eczematous eruptions. They do not believe that eczema in all instances is based on allergy. The mechanism of sensitization is unknown. Autosensitization has been proved by observation of the development of eczema after contact with serum from other eczematous patches. Wise and Wolf believe that mutation may occur from eczema to one of a group of diseases, such as dermatitis exfoliativa, mycosis fungoides, Hodgkin's disease and leukemia. While hypersensitivity may usually be acquired, they believe that there is often an inborn predisposition. Bacterial and mycotic infections appear to predispose to eczema, but Wise and Wolf doubt that the traditionally listed causes, such as alcoholism, digestive disturbances and endocrine disorders, have been proved to be of any special etiologic significance. Atopic dermatitis should be clearly differentiated from ordinary eczema. The authors list a detailed formulary for the topical and general treatment of patients with eczema.

COMBINATION COURSES OF BISMUTH ADMINISTRATION. T. SOLLMANN, H. N. COLE and K. HENDERSON, J. A. M. A. **111**:2175 (Dec. 10) 1938.

Sollmann, Cole and Henderson and their collaborators advocate the use of combined bismuth preparations in order to keep the concentration of bismuth elevated. At first both a series of injections of a soluble bismuth compound and injections of an insoluble bismuth preparation are given. After two weeks the latter only is continued. This form of treatment is advocated in the treatment of patients with acute syphilis who are sensitive to arsenic, but it may be used also in the treatment of early syphilis.

SENSITIZATION REACTION TO SULFANILAMIDE. E. B. ROGERS, J. A. M. A. **111**: 2290 (Dec. 17) 1938.

Rogers reports the case of a woman aged 58 who had previously had several local allergic reactions to injections of procaine, tutocain and butyn. After a recurrent attack of erysipelas, sulfanilamide therapy was instituted. Twenty-five grains (1.6 Gm.) of the drug was taken orally in thirty-six hours. This was followed by swelling and redness of the eyelids, lacrimation and associated pruritus. An area of swelling and erythema was noted in the left groin. Similar lesions appeared at every site of previous application of a local anesthetic. After five weeks the condition had ameliorated. Rogers noted that sulfanilamide and the local anesthetics previously used all had a similar base, aminobenzene (aniline). A drug taken by mouth thus produced flare-up reactions at the sites of injections made years before.

ALLERGY IN CHILDHOOD: III. ITS ONSET AND NATURAL PROGRESS. B. RATNER, J. A. M. A. **111**:2345 (Dec. 24) 1938.

According to Ratner, eczema is the prevailing allergic syndrome in infants under 1 year of age. Food sensitivities were demonstrated in every child who was tested, but further study demonstrated that the predominant allergen in 59

per cent of cases was an "environment contact." Sensitization in utero may not be uncommon. Ratner avers that the onset of allergy may in a measure be prevented through control of the diet of the pregnant woman and of the young infant.

ACTUAL SITE IN SKIN OF INTRADERMAL INJECTION. F. W. TAYLOR, J. A. M. A. **111**:2475 (Dec. 31) 1938.

Taylor enlisted the help of several colleagues, and the skin of various animals as well as human skin was used as the site of intradermal injections of india ink. Sections of the typical bleb produced in every case revealed the ink to be entirely in various depths of the corium. This work indicates that an injected fluid is seldom inoculated into the epidermis even when an intradermal (extremely superficial) injection is given.

PROGNOSIS OF SYPHILIS. H. J. MORGAN, J. A. M. A. **112**:311 (Jan. 28) 1939.

In patients with asymptomatic syphilis the incidence of cardiovascular lesions and of involvement of the central nervous system is greater than in patients who react at the time of infection with acute lesions of the skin and mucous membranes. The threat of untreated syphilis is great. The earlier the infection the greater the menace to exposed persons. Among women with untreated syphilis in pregnancy a healthy baby may be expected 1 time in 6. Infected infants commonly die. The Negro male is vulnerable to cardiovascular lesions and the white male to neurosyphilis. Acute syphilis is curable in from 90 to 100 per cent of patients. From 70 to 80 per cent of patients with early latent syphilis need never suffer from any sequelae of the disease. In cases of late latent syphilis treatment decreases the incidence of damaging lesions.

THE TREATMENT OF VENEREAL LYMPHOGRANULOMA WITH SULFANILAMIDE. A. A. KNIGHT and V. C. DAVID, J. A. M. A. **112**:527 (Feb.) 1939.

Knight and David report the cases of 2 patients with active lesions of venereal lymphogranuloma which had proved refractory to various methods of therapy. In both cases, a favorable result was obtained after treatment with sulfanilamide administered with rest periods over several months.

SULFANILAMIDE THERAPY IN ACTINOMYCOSIS. E. M. MILLER and E. H. FELL, J. A. M. A. **112**:731 (Feb. 25) 1939.

In an 11 year old boy, who had a swelling in the abdomen, spontaneous rupture of the swelling occurred. In the contents liberated onto the skin, granules of Actinomyces were demonstrated. In spite of treatment by means of thymol, potassium iodide and roentgen rays, the process extended, the patient rapidly lost weight and recovery was considered improbable. Miller and Fell then instituted sulfanilamide therapy, and within a week's time improvement was noticed. Treatment by sulfanilamide was continued for almost ten months, at the end of which time the boy had completely recovered.

DERMATITIS DUE TO BUTYN. H. J. PARKHURST and J. A. LUKENS, J. A. M. A. **112**:837 (March 4) 1939.

A 2 per cent solution of butyn was instilled into the eye of a 49 year old woman for local anesthesia. A dermatitis of the lids developed, which in two days caused the eye to be swollen and shut. The condition responded to treatment and was entirely gone in a week. Patch tests elicited a positive reaction to butyn and negative reactions to other possible allergens.

SULFANILAMIDE TREATMENT OF ERYSIPELAS. J. NELSON, H. RINZLER and M. P. KELSEY, J. A. M. A. **112**:1044 (March 18) 1939.

During the first six months of 1937, at Bellevue Hospital, New York, Nelson, Rinzler and Kelsey treated 344 patients with erysipelas by means of administration of sulfanilamide in addition to routine nursing and medical care. Comparing the results obtained by that treatment with those obtained in a series of 4,473 patients with erysipelas treated during 1930 through 1936 by methods not including sulfanilamide, the authors show that sulfanilamide decreased the average duration of the disease and lowered the mortality. In the series in which sulfanilamide was given, the mortality was 2.62 per cent, in contrast to 8.4 per cent in the control series. The mortality in children was reduced from 19.7 per cent in the control series to 12.9 per cent in the patients to whom sulfanilamide was administered.

SYPHILIS AND THE LAW, WITH A DISCUSSION OF THE FALSE POSITIVE BLOOD SEROLOGIC TEST. J. H. STOKES and N. R. INGRAHAM JR., J. A. M. A. **112**: 1133 (March 25) 1939.

Some of the pitfalls which may follow legislative attempts to control venereal diseases are discussed by Stokes and Ingraham. They stress the need for careful study before laws are enacted. No single test or single procedure uncontrolled or unchecked should be used as a basis for a diagnosis of syphilis, including even the dark field identification of Spirochaeta pallida. Serologic syphilis may have no significance for public health, while a patient with a primary lesion still in the seronegative stage may be a public danger of the first magnitude. There is no absolute definition of noninfectiousness, and at present there is no means of attaining it infallibly. Provisions for the changing status of a patient with the institution of treatment should not be incorporated in laws; the decision as to fitness is rather an individual problem. The possibility of a false positive reaction to the serologic test for syphilis should be remembered. The source of the report, the time of withdrawal of the blood and the presence of intercurrent and especially of febrile infections are all important factors in the investigations of the positive report. The clinical examination in the doubtful case must be carefully performed by one familiar with the stigmas of congenital syphilis and with the physical signs of invasion in the acquired form of the disease.

AN OUTBREAK OF ANTHRAX INFECTION IN MINKS WITH INFECTION OF A RANCH OWNER. H. PINKERTON, J. A. M. A. **112**:1148 (March 25) 1939.

Pinkerton reports an outbreak of anthrax in a herd of minks which proved rapidly fatal to more than half. Several were infected in a second herd. The infection was traced to a common source of horse meat from which positive cultures were readily obtained. The owner of the first ranch became infected three days after pelting the last of his minks. Treatment consisted of serum in repeated doses and of neoarsphenamine. Recovery was prompt. No previous records of this infection in minks had been made.

SPONTANEOUS FEVER THERAPY IN NEUROSYPHILIS. F. E. WEATHERBY, J. A. M. A. **112**:1248 (April 1) 1939.

A woman of 31 became disorientated, had convulsions and showed symptoms of tetany, without previous symptoms. There was an associated hyperpyrexia, the temperature reaching 106.4 F. (rectal). The Wassermann reaction of the blood and that of the spinal fluid were strongly positive. The colloidal gold reaction of the spinal fluid was 5553100000. Therapy with tryparsamide was started on the third day and improvement in the condition of the patient began shortly afterward. After ten days, the patient was symptomatically well and subsequent laboratory

examinations showed that the syphilitic process had subsided. The rapid clinical improvement without residual mental symptoms is attributed by Weatherby to the spontaneous fever as well as to subsequent antisyphilitic medication.

THE CEMENT BURN: ITS ETIOLOGY, PATHOLOGY AND TREATMENT. J. M. MEHERIN and T. P. SCHOMAKER, J. A. M. A. **112**:1322 (April 8) 1939.

The factors producing cement burns are considered by Meherin and Schomaker to be (1) abrasive action of the concrete, (2) friction made by wearing apparel and the rubbing of contiguous anatomic parts, (3) heat of solution while slaking, (4) the hygroscopic action of lime with its consequent cellular destruction and (5) its corrosive action as an alkali. The authors treated in the past year and a half 60 cement burns, causing a loss of six hundred and forty-two working days. In 20 per cent of the cases infection developed. Prophylaxis consists in thorough lavage of the exposed parts with water immediately after exposure to cement or concrete, in frequent changing of clothing and in the smearing of the frequently involved parts with a heavy petrolatum ointment.

COCCIDIOIDAL GRANULOMA SIMULATING BRAIN TUMOR IN A CHILD OF FOUR YEARS. B. P. STORTS, J. A. M. A. **112**:1334 (April 8) 1939.

Storts reports the case of a girl aged 4 years in whom symptoms developed over a period of six months suggesting a tumor of the brain. An exploratory operation revealed a large cyst in the cisterna magna with thickened arachnoid. Coccidioides immitis was shown in stained sections. Some improvement followed the operation, and sulfanilamide therapy was given. Death, however, occurred after two months. The autopsy revealed a recurrence of the tumor at the base of the brain and a small nodule in the right lung. This is the first case of coccidioidal granuloma reported from Arizona.

DERMATITIS FROM ORTHODICHLOROBENZENE. J. G. DOWNING, J. A. M. A. **112**: 1457 (April 15) 1939.

Downing reports the sensitivity of a glazier to a solution in which window sashes had been dipped. This sensitivity the author proved by observing the reaction when the substance was dropped on the skin. In a similar manner the harmful ingredient was demonstrated to be orthodichlorobenzene, a substance which has become industrially important in the past few years as a solvent and a wood preservative.

COMPLICATIONS DUE TO ARSENICAL THERAPY IN SYPHILITIC PREGNANT WOMEN: REPORT OF SEVEN MATERNAL DEATHS. N. R. INGRAHAM, J. A. M. A. **112**: 1537 (April 22) 1939.

By an analysis of the records over a five year period of the antepartum syphilis clinic of the Philadelphia General Hospital, Ingraham found evidence to indicate that with certain patients during pregnancy there is a much greater incidence of reactions to antisyphilitic treatment than with others. This evidence is at variance with the teaching of many who consider pregnancy a barrier to harmful sequelae from antisyphilitic therapy. Attention is drawn to 7 maternal deaths following the administration of antisyphilitic drugs reported from six different sources in Philadelphia since 1931.

CHRONIC ULCER OF THE LEG ASSOCIATED WITH CONGENITAL HEMOLYTIC JAUNDICE. E. S. TAYLOR, J. A. M. A. **112**:1574 (April 22) 1939.

In a woman aged 20 with congenital hemolytic jaundice the presenting symptom was a chronic ulcer of twelve months' duration on the inner side of the left ankle. Sixteen days after splenectomy the ulcer was entirely healed, and nine

months later it had remained so. Taylor comments that an ulcer is an infrequent complication but that when present it is extremely obstinate to most forms of treatment except splenectomy, which affords a rapid permanent cure.

TEMPORARILY POSITIVE KAHN AND WASSERMANN REACTIONS IN INFECTIOUS MONONUCLEOSIS: REPORT OF A CASE. J. F. SADUSK JR., J. A. M. A. **112:** 1682 (April 29) 1939.

In a student nurse aged 23, there appeared a sore throat, swollen eyes, a nasal discharge and slight general malaise. There was a slight elevation of temperature. After eleven days a morbilliform eruption appeared and cervical lymph nodes were palpable. The leukocyte count was 6,050 with 65 per cent lymphocytes. Large cells like those ordinarily present in infectious mononucleosis were observed. The sheep cell agglutination test was positive with a dilution of 1:512; later the titer increased to 1:4,096. The Wassermann and Kahn tests showed 4 plus reactions; both became negative in the tenth week of the disease. Sadusk, in reviewing the records at the New Haven Hospital, found that during the past seventeen years, of 37 cases of infectious mononucleosis in which the blood was tested by either the Kahn or the Wassermann technic, in 3 the blood gave false positive reactions. The incidence of false positivity (8 per cent) was thus less than in two other reported series, which showed false positive Wassermann or Kahn reactions in 16 and 60 per cent respectively.

PURPURA HAEMORRHAGICA FOLLOWING USE OF SEDORMID: TWO ATTACKS IN ONE PERSON. T. MCGOVERN and I. WRIGHT, J. A. M. A. **112:**1687 (April 29) 1939.

A white woman aged 57 had taken one-half tablet of sedormid (allylisopropylacetylcarbamide) nightly for several months with no ill effects. After a lapse of about a month she took a whole tablet. Soon afterward she became acutely ill, with chills, fever and excessive thirst, and later a headache developed. When after twenty-four hours the patient was observed by McGovern and Wright, many purpuric lesions had appeared on the skin and in the mouth. They were of various sizes, flat and raised, and in the mouth some were pedunculated. A large hematoma was present on one elbow. A capillary fragility test produced 100 petechial hemorrhages in five minutes. There was a decided leukopenia; the platelet count, which had dropped to 52,000 per cubic millimeter on the fourth day, rose to 140,000 on the seventh day. The vitamin C saturation test gave a normal reading. Treatment consisted in the daily intravenous administration of 1,000 mg. of crystalline vitamin C (ascorbic acid) in 10 cc. of water. Recovery was prompt, but a relapse occurred two months later, when she took one-half tablet of sedormid and showed symptoms similar to those noted.

SYPHILIS, WITH SPECIAL REFERENCE TO THE INCIDENCE IN RELATIONSHIP TO AGE GROUPS AND STATUS OF THERAPY AT THE DATE OF INFECTION. G. H. HANSMANN, J. A. M. A. **112:**1796 (May 6) 1939.

The experience of Hansmann in four sections of the country points to a decided reduction in the incidence of syphilis in the general population. He recently studied at the Milwaukee Children's Hospital the serologic reactions of a series of 3,800 children under 13 years of age and parents, and found that the incidence of syphilis in children was 0.27 per cent. In the generation of those who acquired their syphilis before the advent of knowledge of the spirochete, the development of important preparations of arsenic and bismuth and the knowledge of the serologic tests, the incidence was approximately 12 per cent. Examinations of 4,012 surgical specimens from adults in three years beginning Jan. 1, 1936, revealed evidence of syphilis in only 1 instance. During the same period 178 postmortem examinations were made, and in 8 instances lesions of syphilis were observed. In only 1 instance, however, was syphilis the major cause of death.

Unusual Location of Glomus Tumor: Report of Two Cases. R. C. Grauer and J. C. Burt, J. A. M. A. **112**:1806 (May 6) 1939.

Grauer and Burt report 2 instances in which a glomus tumor developed on the penis. The first patient was a boy of 6 years in whom a grapelike varicosity and a nodule the size of a marble appeared at the site of a bluish discoloration following an injury. The second patient, a man aged 25, had had a small erythematous lesion on the penis since infancy. At 14 years of age he had received a blow on this region, after which the lesion enlarged, assumed the appearance of an angioma and became painful on pressure. In the first case no pain was experienced.

Dermatitis from Industrial Contact with Nicotinic Acid. R. M. Watrous, J. A. M. A. **112**:2132 (May 27) 1939.

Watrous reports the cases of 4 patients who in the course of employment worked with nicotinic acid and shortly afterward had mild degrees of dermatitis on exposed portions of skin. Burning and itching accompanied the rash in 3 instances. Other workers handling nicotinic acid under identical circumstances experienced no trouble.

Lewis, New York.

Two Cases of Miliary Lymphocytoma or Benign Lymphadenoid Granuloma of the Skin. Rupert Hallam and H. R. Vickers, Brit. J. Dermat. **51**:260 (June) 1939. Lymphocytoma of the Face. F. F. Hellier, ibid. **51**:265 (June) 1939.

Of the 3 cases described, 2 were of the localized type of lymphocytoma and the other of the disseminated type. The condition is uncommon, only 20 to 30 cases having been reported. The essential feature is the occurrence of discrete and nonirritating small translucent subepithelial nodules, which histologically are found to be structures resembling lymph follicles and composed of lymphocytic infiltrates enclosing germ centers. The localized type most often attacks the face; it has occurred in both sexes and at all ages but is more common in women. The lesions may persist for years. In one of the cases, diathermy and refrigeration with solid carbon dioxide gave good results. The blood picture is normal. The lesions must be differentiated from those of such diseases as epithelioma adenoides cysticum and adenoma sebaceum. The name "benign lymphadenoid granuloma of the skin" has been suggested.

Desensitization in the Treatment of Menstrual Intoxication and Other Allergic Symptoms. J. Geber, Brit. J. Dermat. **51**:265 (June) 1939.

Among the conditions which Geber lists as manifestations of menstrual intoxication are acne-like eruptions, perifollicular dermatitis, herpes, poppyseed-sized and larger ecchymoses, erythemas, urticaria and bullous dermatitis. These may be accompanied by systemic symptoms. The blood serum is drawn when the symptoms are at their culmination. Its allergenic nature is proved by the method of passive transfer, but the allergenic substance has not been isolated. From 40 to 50 cc. of blood is drawn, treated with 0.3 per cent phenol and stored. In the intermenstruum 0.4 cc. of the serum is injected intracutaneously every second day at widely separated symmetric areas, and subsequent injections are made in the same areas. There may be mild local or systemic reactions. In general there was mitigation of the symptoms even at the following menses, and a second series usually brought about full desensitization. The antigen is apparently highly specific for the individual patient, for the administration of serum from another person failed to accomplish desensitization. The author does not state the number of patients that were treated.

Rattner, Chicago.

DIPHTHERIA OF THE VULVA IN CHILDREN. V. A. PETROVA, Vestnik ven. i dermat., 1939, nos. 2 and 3, p. 71.

Attention is called to the fact that in spite of the frequent incidence of diphtheria of the vulva in girls, with its characteristic clinical picture, the diagnosis is frequently missed. The author reports his observations on 13 cases of diphtheria of the vulva in girls 1½ to 8 years of age. The most characteristic symptom seems to him the complete retention of the urine; this symptom was present in 8 cases, while in 5 there was no retention because pain on urination was less severe. Objective signs are edema of the vulva and dryness and a bluish color of the tissues. In some places the tissues are ulcerated and covered with white and gray membranes the removal of which bares a bleeding surface. In cases of more severe involvement there are areas of necrosis. These manifestations are particularly pronounced in the region of the urethral opening, which seems to be the main reason for the painful urination. The discharge from the vulva was bloody in 9 cases. In 3 cases, in which the condition was less severe, the discharge was insignificant and more purulent, and there was no formation of membranes. In these cases the diagnosis of diphtheria was thought of because of the dryness and the cyanosis of the tissue. In another case the discharge was abundant and purulent, but the dryness of the vulva and the fact that one of the other children had diphtheria of the throat suggested a diagnosis of diphtheria in that individual too. In this case there was an associated gonorrheal infection. Another fairly constant sign is enlargement of the inguinal glands. Association with diphtheria of the throat seems to be rare, occurring but once in the author's cases. General intoxication, malaise and even increase in body temperature are frequently absent in diphtheria of the vulva. In the case of 2 sisters, in spite of a laboratory report of "suspicious of diphtheria," a diagnosis of diphtheria was made because of the characteristic picture, the infectiousness of the disease and the improvement following specific treatment. In another case, in which there were only local symptoms and the clinical course was milder, a diphtheroid bacillus was found. The author believes that the diphtheria bacillus may change its morphologic picture and assume the form of a diphtheroid bacillus, which, although considered nonpathogenic, may under favorable conditions produce a pathologic process of the vulva resembling true diphtheria.

In 10 of the 13 cases there was a preceding chronic vulvovaginitis. The author believes that diphtheria of the vulva develops most frequently as a secondary infection superimposed on a still present or on a past chronic gonorrheal vulvovaginitis.

The prognosis is poor only for patients with severe symptoms or for those who are neglected. In only 1 of the author's cases were there severe complications, and in that case there was no associated diphtheria of the throat.

The author reports also 3 cases of diphtheria of the penis, a disease which is much rarer than diphtheria of the vulva. As in the disease in the female sex, there were retention of urine, the characteristic picture of the tissues and a discharge.

Society Transactions

MANHATTAN DERMATOLOGIC SOCIETY

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May 9, 1939

Minor Congenital Ectodermal Cutaneous Defect in Naevus Linearis Distribution. Presented by DR. MAURICE COSTELLO.

B. O. C., a girl aged 6 weeks, at birth presented a linear ulceration on the left upper extremity, beginning over the deltoid muscle at the tip of the acromion process of the scapula and running along the external aspect of the left arm, forearm and wrist and the dorsal surface of the second and the third finger. It was widest at its origin, measuring 1.25 cm., and tapered to its narrowest portion at its most distal point, where its width was about 0.25 cm. It healed in two weeks, the resulting linear scar involving the site of the previous defect. The Wassermann reactions of the blood of both the child and her mother were negative. She is the first child, and there was no trauma at her birth, which was normal. There is no family history of congenital anomalies.

DISCUSSION

DR. GEORGE C. ANDREWS: I agree with the diagnosis as presented, because if a child is born with absence of skin over a certain area there is a congenital ectodermal defect. In the dermatologic literature the term congenital ectodermal defect designates a clinical entity and is applied to the condition of patients such as those described by Dr. MacKee and me, who have a peculiar facies and absence of cutaneous appendages. In the pediatric literature, however, many circumscribed conditions are classified as congenital ectodermal defects. Dr. MacKee and I described only one kind of congenital ectodermal defect, but there are many localized and minor kinds.

DR. DAVID BLOOM: In this case the name congenital ectodermal defect is appropriate, for, as in most such cases, the condition occurred intrauterum. The other type of condition should be called hereditary ectodermal defect.

DR. GEORGE C. ANDREWS: I think the familial side of ectodermal defects is being stressed too much. If I remember correctly, such conditions occur in families in which there are a great many children, and it is the last one of seven or eight children who has the anomaly. Also, in families that have many children, sometimes the children have many children, and this condition always tends to occur in the last child. It is a sort of degenerative and "worn-out" process. It is not passed on in families as commonly as is psoriasis or epidermolysis bullosa.

DR. MAURICE COSTELLO: This infant was seen by me the day after her birth. A number of such conditions have been described in the literature and have been divided into two classes, minor and major ectodermal defects. The defect in the case presented would be included in the former group, and congenital ectodermal dysplasia has been described under the heading of major defects. MacKee and Andrews reported cases in which there was absence of the skin of the abdomen.

Others have described similar defects on the knees and elbows. They are seen most frequently on the scalp and on the lateral aspects of the arms and abdomen. Scars present at birth in some of these cases indicate prenatal healing.

Psoriasis and Granuloma Annulare. Presented by DR. GEORGE C. ANDREWS.

B. W., a white woman aged 19, states that since she was 2 years of age all the nails of her fingers and toes have been thickened and fragile. For many years the process seemed quiescent; then, at the age of 13, it became active again. The patient complained of dandruff for several years. Except for recurrent attacks of rheumatism she has felt well.

When first examined in 1933 all the nails showed thickening, with accumulation of subungual detritus. The distal portions presented a chalklike appearance. There was periungual swelling with well defined erythema and scaling, and long superficial fissures on the flexor and extensor surfaces of the distal phalanges. No vesicles or pustules were noted. The glabrous skin in general was clear.

In June 1937 smooth flat-topped skin-colored papules developed on the elbows. Histologic examination of one of these papules showed decided hyperkeratosis and acanthosis. The corium was the site of a severe acute and chronic inflammatory reaction, with large numbers of polymorphonuclear leukocytes. There were also edema and a few eosinophils. The changes were not those of granuloma annulare or psoriasis. If the clinical picture were that of an annular granuloma, one could only call the condition erythema elevatum diutinum. The pathologic changes were those of localized cellulitis such as is seen about an inflamed follicle, although no folliculitis was noted in the specimen. The only tenable diagnosis was localized granuloma and cellulitis.

In March 1938 a second biopsy specimen was removed, from the region of the left elbow. This section showed hyperkeratosis and acanthosis. The corium showed some thickening of the blood vessels and a moderate increase of mononuclear cells, and there was some edema, particularly in the papillary layer. No histologic diagnosis was made.

In April 1938 a third biopsy specimen was removed, from the right elbow. The section showed hyperkeratosis and parakeratosis. Parts of the granular layer were well developed. In other places the granular layer had practically disappeared. Edema and canthosis were present. The corium contained dilated vessels and was edematous. An intense infiltrate of polymorphonuclear leukocytes was noted, particularly beneath the epidermis, where the leukocytes seemed to form abscesses with deposition of fibrin. The changes were not characteristic of psoriasis, although they were consistent with one form, known as psoriasis osteacea.

Direct examination of the nails and cultural examination showed no fungi. Cultures of material from the tongue and from the stool for Monilia gave negative results.

Four successive tests with old tuberculin varying in strength from 1:1,000,000 to 1:25,000 gave negative results. After the last test a fine papular eruption developed on the face, and the patient refused further tests.

Roentgen examination of the long bones of the fingers showed moderately large vascular foramens in the distal third of the left fifth and fourth digits, second phalanx, and the right second and fourth digits, second phalanx. The size of the foramens suggested the possibility of early changes of sarcoid.

Treatment has consisted of unfiltered roentgen rays given weekly in doses of 100 r. The lesions on the glabrous skin have been treated with chrysarobin and other reducing agents, without benefit.

Weekly treatments of the nails by iontophoresis were carried out for seven months in 1934, zinc sulfate being used at the positive pole and sodium salicylate at the negative pole. There was no improvement from this therapy.

Weekly injections of dermatomycol were tried for eighteen months, without benefit.

DISCUSSION

DR. DAVID BLOOM: I am unable to make a definite diagnosis, but I have the impression that the lesions on the elbows are scars. As they have been present, together with the ungual changes, since infancy, I should consider the whole syndrome a congenital or inherited dystrophy of the skin and nails.

DR. FRED WISE: Although at present there is no evidence of vesicular or bullous lesions, I believe that the dystrophic form of epidermolysis bullosa as described by Siemens should be kept in mind. It would be of interest to examine the microscopic changes in the elastica.

DR. PAUL E. BECHET: I do not agree with the diagnosis of granuloma annulare, as in my opinion the appearance of the lesions does not in the least suggest that diagnosis.

DR. GEORGE C. ANDREWS: I am much interested in Dr. Wise's remarks. However, the lesions on the elbow have changed greatly in appearance. When we made the diagnosis of granuloma annulare we did it from the clinical appearance of the lesions. They were semicircular, definitely raised, slightly pinkish but almost skin colored, with raised coalescent papules around the border much like those of granuloma annulare. Histologically Dr. Machacek thought that was the most likely diagnosis. The changes in this case occur very slowly. Perhaps later we shall be able to establish a diagnosis.

Dermatitis Herpetiformis Treated with Sulfapyridine. Presented by DR. MAURICE COSTELLO.

A. C., an unmarried woman aged 21, has had Duhring's disease for four years. She had typhoid fever in 1933. Tonsillectomy was performed in 1936. Pneumonia occurred and was treated with pneumococcus serum five years ago. She has chronic otitis media on the left, accompanied by a discharge. The eruption and the subjective symptoms were typical of Duhring's disease. She also had vesicles on the conjunctival sac, on the nasal and buccal mucous membranes and in the external auditory canal. The itching was intense. The phytopharmacologic index was 62 per cent. She had been treated previously with solution of potassium arsenite U. S. P., 10 drops three times a day, which always controlled the eruption, and sunlight, to which she responded fairly well. Roentgen rays, ultraviolet rays, autohemotherapy, intravenous administration of sodium cacodylate, autogenous vaccine from the stool (from Streptococcus viridans and nonhemolytic Bacillus coli), sedatives and cowpox vaccination had no therapeutic effect.

A year ago she was given 40 grains (2.59 Gm.) of sulfanilamide daily for ten days without benefit. About April 15, three weeks ago, she was given a 7½ grain (0.48 Gm.) tablet of sulfapyridine three times a day with 30 grains (1.94 Gm.) of sodium bicarbonate. During the first week of this treatment the vesicles began to disappear and the itching was relieved. At the end of the second week the itching, vesicles and bullae had disappeared, even though the dose had been reduced to 2 tablets a day. The dose has been reduced gradually so that at present she is receiving half a tablet every other day.

DISCUSSION

DR. ISADORE ROSEN: I think the clinical result in this instance is excellent, but I fear that after the drug has been discontinued for two or three weeks the lesions will reappear. That has been my experience.

DR. MAURICE COSTELLO: Sulfapyridine was tried empirically. The patient had previously been told to avoid sunlight, so that her present prompt remission cannot be ascribed to it.

NOTE.—On November 23 there had been no recurrence of the eruption.

Congenital Defects of Skin, Eye and Bones. Presented by DR. GEORGE C. ANDREWS.

J. R., a white girl aged 6 years, at birth had all of the lesions which are now present. The child developed poorly, being of small stature and having extremely wide hips. The left eye is much smaller than the right and is affected by congenital glaucoma. The skin has always been excessively dry and mottled by erythematous and telangiectatic patches and by small flat-topped angiomatous papules. On the arms and trunk there are streaked and linear vesicular lesions somewhat suggestive of angioma serpiginosum, especially in the popliteal spaces. On the sides of the trunk, particularly the right, there is notable atrophy in addition to these vascular changes, and the appearance of this area is characteristic of poikiloderma. Along the forearms and upper parts of the arms, particularly on the anterior aspect of the upper part of the right arm, there are cherry-sized and smaller rounded tumor-like masses which are rather soft. These vary from lemon yellow to cream color. Many are distributed in a linear fashion. On the vertex there is an area of total atricia the size of a half-dollar, and some of the toes are webbed. Roentgen studies have shown that the skull is of normal structure. Measurement between the clinoid processes shows them to be 9 mm. apart.

DISCUSSION

DR. MAURICE COSTELLO: I saw this patient about a week ago. Besides the bizarre lesions mentioned, several fingers are missing, surgical amputation having been necessary because of their flaccidity.

DR. ISADORE ROSEN: Although I am not able to make a definite diagnosis, I suggest that investigations be directed toward examination of the skull for a disturbance of the pituitary gland. Lesions of this kind are associated with such disturbances.

DR. E. WILLIAM ABRAMOWITZ: The elevated lesions in the axilla have a yellowish tinge, as if there were some lymph fat or elastic tissue tumors of some kind. I think that defect could be classed as a very extensive complex hemangioma.

A Case for Diagnosis (Atypical Erythema Induratum?). Presented by DR. PAUL E. BECHET.

H. D., a woman aged 27, is presented from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital. She states that for two years she has noticed on the posterior aspect of both legs a symmetrically distributed eruption which during that period has been constantly present. The eruption consists of two patches of approximately the same size, 15 cm. in diameter. The patches are made up of aggregated red to yellowish papules ranging in size from that of a pinhead to that of a lentil. Some are covered with crusts, others have undergone necrotization and still others are somewhat violaceous. A few punched-out varioliform scars can be discerned. The histopathologic diagnosis was papulonecrotic tuberculid.

DISCUSSION

DR. FRED WISE: Though the large lesion looks more like syphilis than tuberculosis, I should accept the diagnosis of a superficial form of Bazin's disease.

DR. DAVID BLOOM: The edge of the lesions in particular is yellowish red and suggests tuberculosis luposa cutis.

DR. PAUL E. BECHET: There is punctate scarring throughout the lesions. The whole process is superficial, and there are no deep infiltrations. It is Bazin's disease, but the lesions are atypical.

Erythroderma Psoriaticum Cured with 30 per Cent Sulfur in Petrolatum: Coincident Chronic Lymphatic Leukemia and Recurrent Herpes Zoster.
Presented by DR. E. WILLIAM ABRAMOWITZ.

Mr. H. R., a private patient aged 55, married, was a cabinetmaker. He was born in Austria but has lived forty years in the United States. His past history is irrelevant except that he had psoriasis about thirty years ago. During this time he has had six or seven outbreaks of a generalized type. The outbreak under discussion was very severe and developed about January. It was accompanied by an infection of the upper respiratory tract.

At this time it was discovered that the patient had an enlarged liver and spleen with enlargement of the inguinal and axillary glands. The blood count indicated chronic lymphatic leukemia.

The exfoliative dermatitis was treated with a sulfur ointment (30 per cent) in petrolatum. The use of the ointment was continued for a little over three months, resulting in complete disappearance of the eruption. At present only a few scattered scaly papules are present on the body. The sulfur seemed to control the itching better than other remedies.

The blood count now shows: hemoglobin, 69 per cent (10 Gm.); red blood cells 3,700,000 per cubic millimeter, and white blood cells, 38,900 per cubic millimeter, with polymorphonuclears 10 per cent, lymphocytes 86 per cent, monocytes 2 per cent, eosinophils 1 per cent, basophils 1 per cent and normoblasts 1 per cent. The patient is receiving roentgen therapy over the liver and spleen. He is still using the 30 per cent sulfur ointment for the occasional psoriasis papules.

A biopsy specimen taken when the exfoliative dermatitis was present was studied by Dr. David Satenstein who thought that it showed typical psoriasis.

Another feature in this case is that the patient has had ten outbreaks of herpes zoster on the right buttock during the past three years. The remains of a recent attack are still present.

DISCUSSION

DR. GEORGE M. LEWIS: This is a remarkable result. Such conditions have always given me considerable difficulty so far as therapy is concerned. The use of 30 per cent sulfur ointment would seem to be a preferred method of treatment for many types of generalized eczematous eruptions.

DR. ANTHONY C. CIPOLLARO: May I ask Dr. Abramowitz whether he has cleared up ordinary psoriasis with 30 to 40 per cent sulfur ointment?

DR. LUDWIG OULMANN: I saw a colleague with psoriasis lasting for thirty years which responded to treatment at intervals. When leukemia developed (from which he finally died) the psoriasis disappeared.

DR. ISADORE ROSEN: The frequent association of recurrent herpetic eruptions in Hodgkin's disease is well known. I am not aware of such an association with leukemia.

DR. MAURICE COSTELLO: It is not infrequent to see at the Willard Parker Hospital extensive gangrenous herpes zoster varicelliformis occurring in association with Hodgkin's disease. Because of the aberrant vesicles the patients are sent to a hospital for persons with contagious diseases with the diagnosis of varicella.

DR. E. WILLIAM ABRAMOWITZ: An erythroderma following psoriasis may clear up rapidly or may be persistent, so it is difficult to judge the effectiveness of the sulfur preparation. The eruption in this case subsided under the treatment. The patient found that the concentrated sulfur gave him relief from intolerable itching, whereas other antipruritics failed.

For ordinary psoriasis 30 per cent sulfur ointment is not so effective. This seems to apply also to the so-called pustular types. I tried it in a few cases of parapsoriasis, and it was not successful. I have been using it for pityriasis rosea with good results. Oppenheim tells me that its use has been the standard treat-

ment in Vienna since Neumann's time. Patients with pityriasis rosea use it, and in most cases the eruption clears up in two to three weeks.

In the cases of Hodgkin's disease observed by me, the herpes zoster was accompanied by scattered vesicles. I think that I saw the patient referred to, who had sacroiliac herpes zoster and Hodgkin's disease, proved by biopsy. He also had scattered vesicles on the trunk which the Board of Health diagnostician called chickenpox. I disagreed with that opinion.

The patient presented tonight, according to the hematologists, has definite lymphatic leukemia. The recurrent herpes of the left buttock may be herpes simplex, but on account of the pain that develops with each recurrence may be recurrent herpes zoster.

Epidermolysis Bullosa Hereditaria. Presented by DR. MAX SCHEER.

Mr. R., an unmarried clerk aged 35, born in Alsace-Lorraine of Jewish parents, was first seen yesterday at the Mount Sinai Hospital. The condition is said to have been present since infancy. His mother is living and is said to have the same condition, which has diminished in severity as she has grown older. No other members of the family are known to be affected.

The patient's health has otherwise been always good. He had measles as a child. He sweats a great deal, especially his feet and hands. The lesions were at first attributed to trauma in "the cradle." Later, pressure from shoes and tools produced lesions on the feet and hands. These lesions are said to have ranged in size from that of a pea to that of an egg and to have contained clear or bloody fluid. The patient is certain that the frequency of appearance of new lesions is less with the onset of cooler weather.

At present the feet are cool and moist. The soles and sides of the feet and the toes are bluish red. There are areas of callus-like hyperkeratosis on the plantar surfaces of both feet, in the region of the anterior arch; the sides of the feet and the heels are also hyperkeratotic. The toe nails are yellow, opaque and lusterless. There is some maceration between the toes.

There are pea-sized deep-seated hemorrhagic blebs, one on the right foot and one on the dorsum of the foot, just proximal to the web of the great toe. On the mid-dorsum of the same foot is a ruptured bean-sized lesion which contained clear fluid. The left foot shows one lesion on the dorsum, about the size of a pea. The lesions are said to heal in three or four days.

No definite scars are seen on the feet, on the hands or elsewhere. No bullae have appeared on the hands for several months, because the patient has avoided trauma. No lesions have been present at any time on the elbows or knees. No nails have been lost from the fingers or toes.

Since March 1938 the patient has been receiving two intramuscular injections of vitamin C (0.1 mg. each) daily. He is positive that since that time his lesions have been 50 per cent less frequent. Oral administration of the vitamin, according to the patient, was much less effective.

Examination of scrapings for tinea was done but gave negative results.

DISCUSSION

DR. FRED WISE: I do not agree with the diagnosis as presented. I believe that the eruption is due to hyperhidrosis and that the bullous lesions result from occluded sweat gland ducts. By a determination of the hydrogen ion concentration of the fluid from the bullae one might be able to differentiate between sweat and serum.

DR. DAVID BLOOM: As the patient has had this disease since infancy and as the mother has the same disease, the diagnosis of epidermolysis bullosa is to be accepted. Being the simple type which does not leave scars, it is dominant in hereditary transmission. The dystrophic type is transmitted by the recessive mode of inheritance, which explains the fact that in cases of the dystrophic type no other members of the family are usually affected.

Purpura Annularis Telangiectodes. Presented by Dr. Anthony C. Cipollaro.

F. V., a man aged 35, is presented from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital. He complains of an eruption of eight years' duration, involving mostly the lower extremities. The condition has become progressively worse, and there have been no subjective symptoms. The patient has always been in good general health.

The patient has lesions on the legs and on the medial and lateral surfaces of the thighs. The lesions are purpuric and are arranged either as circles or as parts of circles. Some of the circinate lesions are 1 cm. in diameter. The part of the eruption situated on the legs is sharply demarcated. Small areas of atrophy, depigmentation and alopecia are seen. The lesions on the thigh are of the same nature.

DISCUSSION

Dr. Fred Wise: Although the eruption possesses some of the features of Majocchi's disease, it is difficult to determine the diagnosis after a single brief examination. In cases of Majocchi's disease one usually obtains a history of remissions and exacerbations, sometimes associated with rheumatoid symptoms. It would be desirable to examine the blood vessels for hyaline degeneration.

Dr. Anthony C. Cipollaro: I saw this patient a few days ago, and the first diagnosis I made was Majocchi's disease. I looked at the man closely and found that he had definite areas of punctate atrophy. The atrophic spots appeared to be the end results of the purpuric lesions. I saw discoid and circinate lesions with central areas of atrophy. The cayenne pepper spots did not impress me, because such spots are found in any purpuric eruption, whether it is purpura simplex, Schamberg's disease or Majocchi's disease. The general health has been good. The patient has no rheumatic manifestations. There have been no exacerbations or remissions. The disease has become progressively worse and more extensive. Tonight the patient shows lesions in all stages of evolution. Clinically I think that this is a case of Majocchi's disease.

Lichen Planus Starting on the Palms. Presented by Dr. Ludwig Oulmann.

A. W., aged 54, a machinist working with oil a good deal, noticed an itchy rash on both palms four months ago. The lesions were hard papules, and some showed central depression. The lesions spread over the dorsal sides of the hands to the wrists, then to the sacral region and finally to the arms and trunk. In these regions the lesions are scaly. There are annular lesions and longitudinal lesions showing Koebner's syndrome after scratching. There are white plaques on the mucous membrane as well as papules in his mouth.

The patient was seen by us in February but was sent to a physician who treated him as a "compensation case" for an occupational dermatitis. The patient appeared again yesterday in his exacerbated condition. He blames the oil which he is handling. There is no pigmentation.

DISCUSSION

Dr. E. William Abramowitz: This is one of the most pronounced eruptions of lichen planus with palmar lesions that I have seen in a long time.

Dr. Wilbert Sachs: There are some lesions on the chest which are smaller, lack the color of the other lesions and might fit in with the picture of lichen nitidus. I suggest a biopsy of material from these lesions as well as from one of the typical lichen planus lesions.

Dr. Ludwig Oulmann: I could not see any lesions of lichen nitidus. The patient is convinced that the oil which he handles is the cause of his affliction. It is known that dermatitis lichenoides and Riehl's melanosis occur in persons who work with oils, but this is a case of clearcut lichen planus with oral lesions.

CLEVELAND DERMATOLOGICAL SOCIETY

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Feb. 23, 1939

Xanthoma Diabeticorum Chiefly Limited to the Palms. Presented by DR. W. F. SCHWARTZ.

M. D., a woman aged 51, was first seen in the dermatologic clinic at the City Hospital on Feb. 16, 1939, complaining of yellow streaks in the palms. She stated that these had been present for five months. She was known to have had diabetes for nearly three years, which had been controlled chiefly by dietary methods except for a period beginning nine months ago, when insulin was given for three months. She admits that since then she has not followed the recommended diet. About one month after the insulin was discontinued the yellow streaks appeared in the palms.

There is an orange-yellow ribbon-like infiltration in all the flexor folds on the fingers, palms and wrists. A nodule 2 mm. in diameter, of similar color, is situated on the tip of the left elbow. There is no surrounding inflammatory reaction. Near the inner canthus on each lower eyelid is a suggestive diffuse yellowish discoloration without induration. Except in these areas the skin and mucous membranes are free from lesions. Examination of the ocular fundi showed no evidence of diabetes.

On Sept. 13, 1938, the value for blood sugar was 229 mg. and that for blood cholesterol 452 mg. per hundred cubic centimeters. Examination of the urine for sugar on Feb. 15, 1939, gave a strongly positive reaction.

DISCUSSION

DR. E. W. NETHERTON: I disagree with the diagnosis. I believe this is a case of xanthoma tuberosum multiplex. This type of xanthoma occurring in diabetic patients is not uncommon. It is not true xanthoma diabeticorum. In that disease the lesions are usually small, with small yellowish apexes which look like purulent exudate. They usually respond to treatment for diabetes. Xanthoma tuberosum multiplex may occur in a person with diabetes, and the xanthomas may or may not show a response to antidiabetic treatment. The blood cholesterol will be increased in xanthoma diabeticorum provided the diabetes is untreated, while on the other hand it may or may not be increased in xanthoma tuberosum multiplex.

Dermatitis Factitia. Presented by DR. GERARD ANTHONY DEOREO.

R. F., a well nourished but neurotic and apprehensive housewife aged 33, presented from the department of dermatology and syphilology, City Hospital, gives a long history of various complaints since 1930. She had a pelvic inflammatory disease in 1932, sacroiliac arthritis in 1933 and an ovarian cyst one year later. Since this time she has appeared periodically in the surgical outpatient department for treatment of "burns" and other minor "accidents."

On the evening of Feb. 9, 1939, some sores appeared on her left arm; more appeared on the following morning while she was waiting in the dermatologic dispensary. She was advised that new lesions would appear, which they did on February 14. Two days later several new areas were involved.

The skin is clear except for lesions on the left arm. These consist of bizarre, geometrically shaped excoriations on the forearm, the hand and each phalanx. They are in various stages. There are several fresh erythematous areas; other areas are vesicular, and still others are covered with fresh eschar.

DISCUSSION

DR. JOHN A. GAMMEL: Has any effort been made to find out why the patient engaged in this practice?

DR. GERARD ANTHONY DEOREO: My associates and I have gone into the history carefully, though we did not make her realize that we were suspicious. I think there is ample evidence that her home life is not satisfactory. She has to do a good deal of work, and she has three children. I believe she produces the lesions to obtain sympathy. I haven't ascertained as yet how she produces the lesions.

DR. JOHN A. GAMMEL: I contend that the process is not hysterical. When one speaks of hysterical cutaneous conditions one refers to eruptions which come on spontaneously. This patient produces the lesions purposely. I prefer the diagnosis of neurotic excoriations, probably produced by her finger nails.

DR. H. A. HAYNES: I do not approve of the diagnosis of neurotic excoriations. When such excoriations occur it is because the patient thinks there is something wrong with the skin. Dermatitis factitia would better describe this disease.

DR. GEORGE HASKEL CURTIS (by invitation): I should classify this as dermatitis factitia.

DR. JOHN A. GAMMEL: No one will object to the statement that the condition is artificial, but it isn't a dermatitis, even in the widest sense of the term.

Pustular Bacterid. Presented by DR. G. W. BINKLEY.

E. I., a man aged 34, in September 1937 had an eruption on the left heel. Several months later a similar process involved the left hand. In July and August 1938 the toe nails of the right foot and left great toe became thickened. Two weeks ago the patient expressed a bead of pus from under several toe nails on the right foot. There has been no itching or pain.

There is a quarter-sized area of scaly skin on the left thenar eminence. The primary element is a deep-seated pustule, which can be seen where the stratum corneum is thin. In other places the corneum is thick. On the left heel and on the lateral edge of the left foot is a similar plaque showing primary subcorneal pustules. Secondary hyperkeratinization is present. The scales are adherent, tough and dry. The inflammatory process spreads peripherally. At times it recedes only to spread again. There is no central clearing of the process. Several nails of the right foot are thickened, and beneath them is dry, yellow detritus.

Cultures on Sabouraud's brain broth and blood agar showed no growth. Direct microscopic examination of scales and of the contents of pustules showed no fungi or bacteria.

Fungicides and superficial irradiation have been used, but no definite improvement has resulted. In fact, the eruption has spread outward on the heel from an area the size of a silver dollar to its present extent (5 by 10 cm.).

DISCUSSION

DR. C. L. BASKIN, Akron, Ohio: I should make a diagnosis of pustular psoriasis.

DR. JOHN A. GAMMEL: There is involvement of the nails. Unfortunately the patient has been so well treated that it is impossible to see what the original con-

dition was. However, since the nails look so smooth, I think the process did not go through the entire thickness of the nails, probably only the upper third.

DR. H. J. PARKHURST, Toledo, Ohio: I believe the possibility of pustular psoriasis certainly should be considered, although the patient is unaware that there has been any eruption in the past. It is possible that the changes in the nails may be psoriatic and that the cutaneous lesions may be pustular psoriasis. However, I favor more the diagnosis of pustular bacterid with periodic flare-ups and erythematous patches. Such conditions are often relieved by tonsillectomy, the tonsils being the common focus of infection. However, I feel that in the presence of involvement of the toe nails one should not entirely abandon the possibility of dermatophytosis.

DR. JOHN A. GAMMEL: Have any efforts been made to find a focus of infection?

DR. G. W. BINKLEY: I have examined the patient's tonsils. They showed no particular abnormality, but I shall consult a specialist in diseases of the nose and throat as to whether a tonsillectomy is indicated.

Melanosarcoma (Cutaneous Melanoblastoma). Presented by DR. HAL ELSON FREEMAN.

C. H., a man aged 72, is presented from the department of dermatology and syphilology, City Hospital. He first noticed growth and enlargement of one of many pigmented nevi on the back five weeks ago. A tendency to bleed easily was noted.

The lesion, which is in the mid-dorsal region, to the left of the midline, is a bluish black, pigmented, slightly raised area measuring 2 by 4 cm. Histologic examination of tissue removed from the center of this pigmented area showed the skin to be resistant to cutting and firm and fibrous to a depth of approximately 1 cm. The surrounding skin shows numerous seborrheic keratoses and melanotic nevi.

Histologic examination showed the epidermis to be thin and atrophic. Near the center of the section was a tumor which invaded the corium. It was composed of variously sized and irregularly shaped cells with vesicular or compact nuclei and varying quantities of basophilic granular cytoplasm. Some of these contained large amounts of brown granular pigment. Other cells had grown out from the main tumor, and small groups of them were observed beneath the basal layer of the epidermis. Some had penetrated the epithelium. Occasional collections of tumor cells were present in the lymphatics of the corium. There was a chronic inflammatory infiltrate along the margins of the tumor.

DISCUSSION

DR. W. F. SCHWARTZ: If one has a suspicion that a melanotic lesion is undergoing malignant degeneration, is one justified in taking off the entire lesion when it is as large as this one, or is it permissible to take material for biopsy from the recently growing part?

DR. E. W. NETHERTON: I feel that if it is a true malignant growth which has undergone recent degeneration, the probability is that when a clinical diagnosis can be made it is too late to do anything for it. Sometimes the clinical impression is wrong, and there is nothing to be lost by doing a wide excision. One may possibly save a life that otherwise would be lost. If the tumor is a melanoma and is left alone, one knows the ultimate outcome. If there are demonstrable metastases, I think it is foolish to do anything in the way of a surgical procedure.

Various pathologists differ regarding the taking of biopsy specimens. I believe that if a specimen is taken with a cautery the risk is not great—that is, in a case of ordinary malignant disease. Melanomas are treacherous. I prefer to excise them and then examine them.

DR. JOHN A. GAMMEL: Some time ago I saw some statistics presented by an English writer on melanomas. He stated that the mortality is 96 per cent. Early radical treatment should improve this rate.

DR. C. G. LAROCCO: I believe that any tampering with a lesion of this type should be done with the plan of excising it completely. As such a tumor is highly malignant and tends to metastasize readily and seriously, the safer plan would be to excise it widely and then get biopsy material from the excised lesion.

DR. E. W. NETHERTON: I heard Dr. Freeman say that such tumors are supposed to come from the mesoderm. I think it is the accepted opinion at present that melanoblasts arise from cells of nerve sheaths.

DR. HAL ELSON FREEMAN: I have read in two recent books that if such a growth is a raised verrucous lesion it usually is a melanocarcinoma. If it is flat or slightly raised, it is probably not epithelial but mesodermal in origin.

DR. H. J. PARKHURST, Toledo, Ohio: In a case of this kind I consider electrocoagulation and intensive treatment with roentgen therapy the method of choice. If metastases have not yet occurred, the growth can be cured. I believe I have cured 2 or 3 patients in this manner.

DR. E. J. ARDAY, Lakewood, Ohio: I do not think there is enough evidence for this diagnosis, and I am inclined not to accept it.

DR. H. A. HAYNES: It is my impression that melanomas are extremely radioresistant. I had a patient a year and a half ago whom I treated with radiation. A total of 8,000 r was given in a small area, enough to cause complete tissue destruction, at least of the surrounding tissues. The melanoma in the center was more resistant than the normal tissue.

DR. H. G. MISKJIAN: About 1935 I read a paper on melanoma (Scharnagel, I. M.: *Acta radiol.* **14**:473, 1933). A physician of Stockholm, Sweden, had collected all the cases of melanoma observed over a number of years. Roentgen therapy had been employed. The diagnosis had been confirmed histologically in each case. The doses had not been high. The results were satisfactory. There was a large percentage of cures. That has puzzled me ever since. It has been absolutely impossible for me to understand how they could get any results with the dosage they used.

NOTE.—I observed, on looking over the article, that a combination of methods was used, including electrosurgery, and not roentgen therapy alone.

Onychia Due to Handling Sugar. Presented by DR. C. L. CUMMER.

A. R., a woman aged 23, complained of a disease of her finger nails, of two years' duration. It began about two or three months after she started to work in a bakery, where she handled jams and jellies, pressing this material with her bare fingers into baked goods as a filling.

When first seen, on July 18, all the finger nails except those on the thumb and index finger of the left hand were affected. Some were entirely stripped off; others were split and lifted from the nail bed. In some instances the distal portions were detached; in others, the proximal. The paronychium around the involved nails was red, swollen and tender. The detached nail tissue was yellow, and the history indicated that some pus had been present. Except in one or two nails,

the nail plates were thinner than normal. When the nail plate was lifted, heaped-up and granular tissue could be broken away.

Microscopic examination of nail tissue showed no mycelium or spores.

A photograph is presented to show the condition when first seen. The nails at present appear entirely normal.

After the patient stopped work the disease responded promptly to treatment with roentgen rays, with compresses soaked in boric acid solution and with boric acid ointment.

This condition is described as "sugar onychia" in Prosser White's book (The Dermatoses or Occupational Affections of the Skin, ed. 3, New York, Paul B. Hoeber, 1929, p. 318).

Onychia due to contact with sugar.

Atrophic Arthritis with Subcutaneous Nodules and Tertiary Syphilis.
Presented by DR. W. F. SCHWARTZ.

J. M., a woman aged 57, is presented from the department of dermatology and syphilology, City Hospital. She has been troubled with a progressively developing atrophic deforming arthritis, affecting chiefly the small joints of the extremities, for the past five years. In the past three weeks two firm, painless nodules have developed in the scalp. The patient stated that three years ago she had similar nodules in the scalp, which lasted about three months but disappeared under the influence of massage.

In the occipital region are found solitary firm painless nodules measuring approximately 0.75 cm. in diameter. They are firmly attached to the underlying structures, but the overlying skin does not appear to be affected. There are no clinical signs of syphilis.

Serologic tests for syphilis gave strongly positive results.

Biopsy was not permitted by the patient.

Atrophic Arthritis with Subcutaneous Nodules and Pulmonary Tuberculosis. Presented by Dr. W. F. Schwartz.

T. C., a man aged 30, is presented from the department of dermatology and syphilology, City Hospital. In the past five years he has had intermittent attacks of arthritis affecting chiefly the joints of the hands, feet, wrists, elbows and knees. The condition was diagnosed as atrophic arthritis. For three years he has had pulmonary tuberculosis. About two months ago three firm, painless nodules measuring from 1 to 1.5 cm. in diameter developed in the scalp, and a similar one developed over the right elbow. One of the smaller ones in the scalp was removed for histologic examination. The nodule over the elbow has also been removed for microscopic study.

The nodules are apparently attached to the underlying periosteum. There is no sign of acute inflammation, and the overlying skin shows no change.

Roentgen examination of the skull showed no evidence of exostoses.

Examination of the sputum revealed tubercle bacilli. Serologic tests for syphilis gave negative results.

Histologic examination of the tissue removed showed essentially no change in the epidermis, the chief change being found deep in the corium and in the subcutaneous tissue in both specimens. It consisted of several small focal areas of necrosis, each of which had a striking peripheral zone of radially arranged epithelioid cells. These areas were separated by incomplete bands of newly formed and old fibrous connective tissue cells with surrounding edema.

DISCUSSION OF CASES OF ATROPHIC ARTHRITIS

Dr. W. F. Schwartz: A good many diagnoses had been suggested, sarcoid, exostoses and the like, before we had the benefit of the slide.

Dr. C. L. Cummer: Are these nodules regarded as similar to subcutaneous fibroid nodes such as are seen in children with rheumatic heart disease?

Dr. W. F. Schwartz: H. Keil (Rheumatic Subcutaneous Nodules and Simulating Lesions, *Medicine* **17**:261-380 [Sept.] 1938) stated the belief that the rheumatic subcutaneous nodules frequently seen in children are essentially the same as the rheumatoid nodules seen in cases like the present one. He dealt with that subject thoroughly. He stated that these nodules may be a sign of an active rheumatic process in children but do not constitute such a sign in the adult condition. Many of the nodules are self limited and may last only a few days to a few weeks at the most and then disappear. These 2 patients point to the fact that subcutaneous rheumatoid nodes are not infrequently seen in the scalp. They usually appear in the articular regions and are believed to be secondary to trauma.

May 25, 1939

Capillaritis. Presented by Dr. Benjamin Levine.

E. N., a white woman aged 50, has been under antisyphilitic therapy for the past six years. During the past two years on the lower extremities numerous diffuse purplish noninfiltrated macular patches have developed which do not disappear on pressure. The subjective sensations are slight.

Histologic examination reveals evidence of subacute inflammation, with moderate endothelial proliferation, an increase in the number of blood vessels and a moderate increase of brown granular pigmentation in the basal cell layers.

DISCUSSION

DR. H. G. MISKJIAN: I am glad to see that the word capillaritis is becoming more popular. I believe the condition in this case is an early form which later will develop into what is usually called varicose dermatitis. The newer name for that is purpuric pigmented dermatitis with thickening of the skin. Anatomically and clinically the lesions are more of the vascular type than of any other.

Mycosis Fungoides. Presented by DR. IRVING L. SCHONBERG.

J. G. S., a man aged 45, has had trouble with his skin for the past thirty-four years. The condition originally started as spots over the entire body, which gradually acquired scales. He was seen by several dermatologists, who made a diagnosis of exfoliative dermatitis. In addition, ring-shaped lesions have developed on the chest. He has also noticed tenderness under the left arm and swelling in the lymph nodes of the groins. The condition for the past few years has been better in summer.

Examination reveals erythematous scaly areas over the face, scalp, back, chest and legs. On the chest, in addition to the scaly lesions there are infiltrated violaceous patches, varying in size from that of a quarter to that of a dollar. Itching has been slight and occasional. From time to time he has noticed small ulcers appearing in the groin.

Serologic tests for syphilis gave negative results. The hemogram is normal.

The patient has been receiving vitamin therapy, has been applying an ointment consisting of 2 per cent salicylic acid in rose water ointment U. S. P. and has been taking starch baths.

Histologic examination of two sections showed the epidermis for a distance of about 14 mm. to be several times average thickness. All but the basal cells were swollen, and the outermost cells in places showed prominent vacuolation. In several places there were definite tiny vesicle formations, the largest about 350 by 150 microns. There was some round cell infiltration in the thickened epidermis. Overlying the epidermis was some desquamated necrotic epithelium. The epithelial prolongations of the epidermis were lengthened everywhere, and there were fairly numerous mitotic figures in the epithelial cells, with no extension beyond the basement membrane. There were moderate to considerable round cell infiltration and scarring in the upper corium. The cutis throughout showed increased reticular connective tissue. There were no sebaceous glands, and the sudoriferous glands showed atrophic changes.

DISCUSSION

DR. J. E. FISHER: I saw the patient about eighteen years ago and made a diagnosis of parapsoriasis. The lesions are now more pronounced, but I still offer the same diagnosis.

DR. I. L. SCHONBERG: I saw this patient about two months ago. At that time he presented a scaly condition, more severe than the present one, over the entire body and some infiltrated nodules on the chest. The main part of the dermatosis was not infiltrated. The diagnosis of dermatitis exfoliativa was made several years ago by Dr. J. Schamberg, of Philadelphia. The condition has progressed somewhat. It has never been the source of itching or any discomfort. The histologic examination showed some of the early changes that one might find in the premycotic stage of mycosis fungoides. He has never had roentgen therapy.

DR. H. N. COLE: I think I saw the patient a couple of years after I was in practice, before Dr. Schamberg saw him. I made the same diagnosis, and the patient went to the Mayo Clinic, where the same diagnosis was again made. His condition has certainly changed since that time. The generalized condition in some

ways makes one think of a nevoid condition or parapsoriasis. The areas on the inside of the right thigh, where he has some lymphangiectasis, resemble those on a patient presented at the Academy meeting in St. Louis last fall. He does have some plaques on the back, about the size of the palm and with a tendency to be elevated at the periphery and to be somewhat depressed in the center, that suggest the beginning of the tumorous stage of mycosis fungoides. When I looked at the slide and saw the sharply defined sleevelike type of infiltrate, I was inclined to think that the condition might be an unusual type of mycosis fungoides that has developed in a parapsoriasis that has lasted all these years. It is hard to understand why he has had so little pruritus.

DR. HUGO HECHT (by invitation): My first impression was that the disease is mycosis fungoides. I saw the patient today for the first time.

Urticaria Pigmentosa. Presented by DR. BENJAMIN LEVINE.

R. T., a Jewish woman aged 35, for the past ten years has had distributed over the trunk and extremities numerous brownish and erythematous macules, varying in size from that of a pinhead to that of a pea. On manipulation these areas become darker and papular. At times the condition is intensely pruritic.

Treatment has been symptomatic.

Histologic examination revealed an infiltration of mast cells in the corium, especially near the basal cell layer. The cells were large and spindle shaped, oval, round or polygonal and were separated from the epithelium by normal connective tissue. There was increased pigmentation in the basal cell layer and also in the papillary body.

Urticaria Pigmentosa. Presented by DR. BENJAMIN LEVINE.

M. R., a pregnant woman aged 29, stated that eight years ago she noticed a rash, which at times was itchy. The eruption gradually became darker and on friction would become edematous and more extensive.

The lesions are sparsely generalized, discrete and about 5 mm. in diameter. Since the patient has become pregnant the eruption has been less pronounced.

Urticaria Pigmentosa. Presented by DR. BENJAMIN LEVINE.

H. K., a woman aged 25, for the past four years has had an itching eruption.

Over the chest and back are numerous split pea–sized brown macules, which become edematous after irritation.

Lymphangiectasia of the Vulva with Edema of the Legs. Presented by DR. FRANK MCDONALD.

M. B., an obese Italian woman aged 52, presented from the department of dermatology and syphilology of the Lakeside Hospital, has symptomless lesions on the vulva of two years' duration. The legs have been swollen for almost twenty years. The swelling in the left leg has been attributed to a fracture, and the swelling in the right leg apparently arose as phlegmasia alba dolens concomitantly with pregnancy.

On the upper portion of the right side of the vulva are ten or twelve grayish vesicopapules, each somewhat smaller than a split pea, grouped together in an area measuring about 2 by 3 cm. There is no evidence of inflammation in the surrounding area. When the individual lesions are opened, a slight serous exudate is obtained. The lower extremities exhibit a pitting edema. There are no scars, varicosities or ulcers, and there is no tenderness.

A blood smear failed to reveal Filaria bancrofti.

Histologic examination of tissue removed from a vulvar lesion showed a thick layer of hyperplastic stratified squamous epithelium. Throughout the cutis and in

the rete pegs was a dense infiltration with small round cells, including plasma cells and lymphocytes. There was a moderate amount of fibrosis. There was no evidence of tumor. The lymph vesicles and spaces were greatly dilated.

Hemiatrophy of the Face. Presented by DR. BENJAMIN LEVINE.

E. B., a woman now aged 59, at the age of 18 was struck on the head with a flatiron, and her skull was presumably fractured. The skin was not broken. Four years later she had her first attack of epilepsy. These attacks lasted for a short time and occurred without aura. They were later controlled by antisyphilitic therapy.

When she was first seen, in September 1932, there was a hemiatrophy of the left side of the face. The skin is atrophic and closely adherent to the bone, with atrophy of the subcutaneous tissue and muscle. There is no paralysis.

The Kline test for syphilis gave a strongly positive result. The spinal fluid was normal.

DISCUSSION

DR. H. N. COLE: I have seen several patients with hemiatrophy of the face. However, the condition is not necessarily localized to the face but may involve other parts of the body. In the large proportion of cases there is a history of trauma. Bartlett has written a great deal on this subject. If it occurs early enough, it may even involve bone, and the bone will not grow as much as the corresponding bone on the other side.

DR. H. A. HAYNES JR.: It is interesting that epilepsy developed in this patient also. A decompression would possibly have prevented the epilepsy.

A Case for Diagnosis (Macular Atrophy? Nonsyphilitic White Spot Disease? Anetoderma Erythematodes of Jadassohn?). Presented by DR. BENJAMIN LEVINE.

L. W., a woman aged 45, has had numerous white spots on the neck, chest, shoulders and back for sixteen years. The condition progressed until the birth of her last child, ten years ago. The lesions are not itchy or painful.

The individual lesions vary in size from 1 to 5 mm. in diameter. They are dead white and atrophic, with great enlargement of the pores, giving a pig-skin-like appearance. The smaller lesions are on the neck; the larger, on the chest and back. There is increased pigment on the right side of the neck.

The basal metabolic rate was —6 per cent. The hemoglobin content was 52 per cent, but the hemogram was otherwise normal. Serologic tests for syphilis gave negative results.

The patient would not allow a histologic examination.

Contact Dermatitis Due to Physostigmine Salicylate. Presented by DR. H. H. JOHNSON.

L. S., a woman aged 59, presented from the department of dermatology and syphilology of the Lakeside Hospital, in February 1937 had a diagnosis of chronic glaucoma made at Lakeside Hospital. She was treated with 1 per cent pilocarpine hydrochloride. Physostigmine ointment, containing 0.5 per cent physostigmine salicylate, was applied only occasionally until Aug. 3, 1937, when she was again given this medication. After one week the eyes and lids became red, and by December 13 there were generalized erythema and scaling of the face. These have persisted, with exacerbations and remissions. On April 15, 1939, an exacerbation of the condition occurred. The ointment was discontinued on April 21, and the dermatitis has been slowly subsiding since that time.

Examination shows a diffuse erythema of the face and neck, with scaling and cracking of the skin. There is moderate edema of the face, especially about the eyes.

The conjunctivas are moderately injected. The optic fundi show glaucomatous disks, and there is an iridectomy window in each iris.

Patch tests with 0.5 per cent physostigmine salicylate gave strongly positive reactions; with 1 per cent pilocarpine hydrochloride, negative; with 0.5 per cent pontocaine hydrochloride, slightly positive, and with 1 per cent phenacaine hydrochloride, negative.

DISCUSSION

DR. H. H. JOHNSON: Contact dermatitis from physostigmine salicylate ointment has been reported infrequently in the literature. Atropine is commonly described as producing an irritation of the eyes. In several recent textbooks on dermatology no mention of physostigmine as a possible irritant is mentioned.

Congenital Syphilis. Presented by DR. BENJAMIN LEVINE and DR. I. L. SCHONBERG.

W. J. B., a Negro boy aged 12 years, whose parents are known to have syphilis, presents Hutchinson teeth, a saddle back nose, a high palatine arch and thickened periosteum over the tibias. The eyes appear normal. His mentality is good, but he is undersized for his age.

Serologic tests for syphilis were strongly positive.

DISCUSSION

DR. J. R. DRIVER: I asked the child whether he had ever had sore eyes. He said that his eyes had been inflamed and red on two or three occasions several years ago. On close examination there is no evidence of interstitial keratitis. However, I believe it would be interesting to have the cornea examined by the slit lamp. In many instances in which nothing is seen grossly, the telltale scarring is evident on slit lamp examination.

Scleroderma. Presented by DR. BENJAMIN LEVINE.

B. M., a man aged 47, noticed hardening and thickening of the skin of the left forearm the latter part of July 1937.

It became progressively more extensive until it involved all of the left shoulder and extended in a broad band, 8 to 10 cm. in width, over the lateral portion of the brachium and the dorsal surface of the forearm, terminating on the dorsum of the index finger.

The skin is smooth and shiny with increased pigmentation and mottled pigmentation over the areas in which the scleroderma first appeared. The lesions also are firm and slightly edematous, with firm attachment to the underlying tissue, resulting in a hidebound condition.

He had received twenty-six injections of solution of posterior pituitary U. S. P., of 1 cc. each. Six months after these injections the condition showed signs of regressing, with decrease in stiffness and edema.

Histologic examination of tissue showed that the papillary bodies were flattened and obliterated. The horny layer was increased. There was degeneration of the connective tissue bundles. The blood vessels showed endoperiarteritis and phlebosclerosis. The hair follicles and glands in certain areas have disappeared.

Papilloma of the Palate (Probably Due to Red Mercuric Sulfide [Cinnabar]). Presented by DR. BENJAMIN LEVINE.

S. H., a man aged 52, has had diabetes for the past eighteen months. For the past year he has been conscious of "lumps" on the hard palate. He has been wearing a red dental plate.

There are numerous enlarged follicular openings on the hard palate. On some areas there are pinhead-sized to split pea–sized erythematous soft papillomatous growths.

Histologic examination showed acanthosis, spongiosis and marked elongation of the papillary bodies. There was thickening of the malpighian layer, with hypertrophy of the interpapillary pegs.

DISCUSSION

DR. J. R. DRIVER: I have observed several patients with stomatitis due to plates, and in the cases I have had, patch tests with the plate itself on the skin have given positive results. I should suggest that patch tests be done in this case.

Radiodermatitis of the Hands with Malignant Degeneration. Presented by DR. H. N. COLE and DR. J. R. DRIVER.

A. A. B., a dentist aged 60, has had an irritation of the fingers of both hands for five years, which he attributed to contact with procaine hydrochloride. He has noticed for several years warty growths on his fingers. One month ago he scraped one of these lesions off accidentally, and the area thus traumatized has ulcerated and has not healed. For a period of more than fifteen years he has taken roentgenograms of teeth.

The thumbs, index fingers and middle fingers of both hands are primarily involved. They show numerous keratoses, with dryness and some atrophy of the skin. The nails on these fingers are brittle and show longitudinal striations. On the dorsum of the middle finger of the right hand is an ulcer 4 by 3 cm., with indurated granulomatous edges.

Histologic examination of a specimen taken from the edge of the ulcer showed that the epidermis was thickened, and in one situation there was ulceration, the ulcer being occupied by tumor. Beneath the epithelial layer was a tumor which had invaded the skin and subcutaneous tissues. It was not encapsulated, and there was obvious local invasion. The tumor was composed of atypical epithelial cells, and in some places there were degenerate epithelial pearls. No intercellular bridges were seen. There were also foci of degeneration and necrosis of tumor cells, which gave some areas a network appearance. The individual cells tended to be round and moderately large with abundant cytoplasm, pleomorphic and hyperchromatic nuclei showing numerous atypical mitotic figures. Surrounding the tumor were moderate fibrosis and infiltration with small round cells. There was no necrosis or hyaline thrombosis of the blood vessels, and no eosinophilic infiltration was seen. A diagnosis of well differentiated squamous cell carcinoma was made.

DISCUSSION

DR. HUGO HECHT (by invitation): In Prague about fifteen years ago (in 1924) I observed a similar condition in a young man. He was treated with roentgen rays. Two years later the ulcer was cancerous. The finger was removed, and then the right arm. The development was from 1922 to 1929. He had about seven operations. Radium may be tried, but surgical treatment is better.

DR. H. N. COLE: Dr. Driver and I have seen several dentists who told in their history of holding dental films in the mouths of patients while taking roentgenograms of teeth. The practice is not carried on so much at present, but it is surprising how often it was done in the past. For many years the patient presented today held films in mouths with his thumb. Apparently this finger got caught in the process and even got a larger dose than the thumb. Typical radiodermatitis, changes in the nails and an ulcer on the back of the hand have developed.

Since the tendon is involved in this case, it will be impossible to cure the process by any method except amputation. I know of no carcinoma on the hands in which the tendons were involved that was cured by irradiation. The finger will be amputated tomorrow.

The question has been raised as to how this condition can be radiodermatitis without telangiectasia. I saw a dentist this morning who has had a similar condition, without telangiectasia, which is now cleared up.

Pityriasis Lichenoides Chronica. Presented by Dr. George H. Curtis and Dr. E. W. Netherton.

S. S., a Jewess aged 32, noticed an eruption first on her face about six years ago and shortly afterward on the extremities; it rather rapidly spread to involve the trunk. There have been no subjective sensations, except for dryness of the skin. The eruption appears to be more pronounced in the spring and fall. All sorts of treatment have been tried without benefit.

The eruption is most intense on the extremities, the face and the lower part of the trunk. On the face there is a slightly scaly reticulated erythema showing telangiectasia on diascopic pressure. Scattered over the trunk and extremities are many split pea-sized flat scaling macules with a yellowish tint, while other lesions are papular, especially on the extremities. The scales on the papules are difficult to remove and leave a pink moist surface underneath. The axillary folds and the upper extremities show a bluish red reticulated erythema and telangiectasis. In the network are pinpoint-sized to pinhead-sized deep red papules simulating those of lichen planus. Distally the network thins out and consists of sparsely distributed erythematous scaly macules, somewhat lichenified. The lower extremities show similar changes. The mucous membranes are normal.

General physical examination showed only normal conditions. The hemogram and the urine were normal. Serologic tests for syphilis gave negative results.

Histologic examination of sections taken from lesions on the hip and the upper part of the arm showed in the horny layer a definite parakeratosis but no corresponding granular layer. The prickle cell layer was acanthotic, with spongiosis and several vesicles in early stages. Small round cells had invaded the epidermis; except where the edema of the papillae had invaded the germinal layers, the basement membrane was intact.

A number of the papillae were considerably flattened below the acanthosis, but many showed edema and round cell infiltration, especially around dilated capillaries.

The upper part of the corium showed edema and small round cell infiltration continuous with that of the papillae. About dilated blood vessels the edema and cellular infiltration were most marked. The infiltrate consisted almost entirely of small round cells. No eosinophils, neutrophils or plasma cells were seen.

The deep corium and the subcutaneous tissue were unaffected.

A section including pinhead-sized papules from the brachium showed similar but less extensive changes, except that the blood vessels of the corium were more numerous and dilated, and there was hyperkeratosis, without parakeratosis.

DISCUSSION

Dr. J. E. Fisher: I had the privilege of seeing this patient five years ago, and the picture has not changed much since that time. I agree with the diagnosis as presented. She had not responded to any treatment at that time, including various topical applications. I made a metabolism test, the result of which was normal.

Dr. H. N. Cole: I think that in some places on this patient's body the discrete papules are rather characteristic of pityriasis lichenoides chronica. Considering the amount of telangiectasia and atrophy, one should keep in mind the possibility of Jacoby's disease as time goes on.

Dr. Hugo Hecht (by invitation): I have seen the best results with six months of sunshine and sea baths. I think Florida has the right climate. In Prague there are two or three families who have this condition. Every summer they go to the seashore, but in the winter the eruption recurs.

DR. J. R. DRIVER: What I have to say is speculative. I think it might be interesting to investigate whether the condition is a deficiency disease. I had in mind the possibility of perhaps using riboflavin in the treatment.

DR. GEORGE H. CURTIS: We presented this case for two reasons. The first reason is that the patient insists that the eruption improves in the summer, seems to be worse in the spring and is bad in the fall and throughout the winter. With that history in mind I should like to ask whether it might be advisable for her to invest in an ultraviolet lamp. The second reason is that Juliusberg in his article says that often the condition when on the extremities must be differentiated from poikiloderma. The eruption on the arms shows some telangiectasia, the overlying epidermis is atrophic and it is deep red. The epidermis and probably the upper part of the cutis seem to be atrophic. On the sides of the neck the eruption has a retiform character and looks like parapsoriasis variegata, particularly as illustrated in Ormsby's textbook (Ormsby, Oliver S.: Diseases of the Skin, ed. 5, Philadelphia, Lea & Febiger, 1937, p. 284).

Necrobiosis Lipoidica Diabeticorum. Presented by DR. E. W. NETHERTON and DR. GEORGE H. CURTIS.

G. C., a housewife aged 37, was presented before the society on Jan. 19, 1939 (ARCH. DERMAT. & SYPH. **40**:455 [Sept.] 1939).

She is shown at this time because (1) the lesions have enlarged and are clinically more suggestive of Boeck's sarcoid and (2) although her diabetes has been rigidly controlled for more than six years, new lesions have appeared and the old ones have enlarged.

On May 24, 1939, the blood cholesterol was 146 mg. per hundred cubic centimeters and the blood sugar (fasting) was 128 mg. per hundred cubic centimeters.

New histologic sections have been stained for fat and elastic fibers and showed the typical histologic changes of necrobiosis lipoidica diabeticorum.

Syphilitic Macular Atrophy. Presented by DR. BENJAMIN LEVINE.

A. H. J., a Negress aged 27, states that a rash developed over the entire body four years ago. She consulted a physician, who made a blood test, which gave a strongly positive result. She received injections in the arm and in the hip for one year.

On the trunk and extremities there are numerous split pea–sized to coin-sized atrophic areas.

Serologic tests for syphilis gave strongly positive results.

Histologic examination of tissue showed that the surface epithelium was somewhat thinner than average. In the corium there was some increase in the relatively acellular fibrous tissue. The cutaneous glands were diminished in size and number. In the upper layers of the corium there was some perivascular infiltration. The section was stained for elastic fibers by Weigert's method and showed no appreciable diminution in their number.

DISCUSSION

DR. H. N. COLE: Syphilitic macular atrophy is not common, but it does occur, particularly in Negroes. Histologic examination does not show evidence of syphilis. The condition is probably the result of some trophic factor.

DR. I. L. SCHONBERG: I should like to ask Dr. Cole in how many patients that present this trophic macular atrophy he would expect to find neural changes in the cord.

DR. H. N. COLE: I am not in a position to answer that, but I think it would be an interesting question to investigate.

DR. GEORGE BINKLEY: In the cases of syphilitic macular atrophy I have observed, the examinations of the spinal fluid have given normal results.

DR. BENJAMIN LEVINE: The patient just presented has normal spinal fluid.

June 15, 1939

Necrobiosis Lipoidica Diabeticorum. Presented by Dr. Gerald Anthony DeOreo.

L. R., a woman aged 29, is presented from the department of dermatology and syphilology, City Hospital. She has had diabetes mellitus since 1933. The disease has been controlled by diet and insulin. About two years ago a lesion developed on the anterior surface of the left leg, which she states resulted from a bruise. It has gradually increased in size.

At present it is about 3 cm. in diameter. The border is violaceous and the center yellowish, with numerous telangiectases.

The value for blood sugar recently has varied from 87 to 187 mg. per hundred cubic centimeters. A urinalysis showed a faint trace of sugar.

Histologic examination showed that the epidermis was thin, the papillae decreased in number and the follicles larger than usual. In the deep layers of the corium the blood vessels and glands were surrounded by fuzzy collars of lymphocytes, a few large mononuclear cells and occasional polymorphonuclear leukocytes. Deep in the corium there were a few strands of young connective tissue sprinkled with chronic inflammatory cells and the collagen fibers were swollen and fragmented. In such areas a few pyknotic inflammatory cells were seen. The results of histologic examination were consistent with the clinical diagnosis.

Livedo Racemosa in a Syphilitic Patient. Presented by Dr. Gerald Anthony DeOreo.

M. S., a woman aged 26, was seen at the City Hospital in 1932, at which time a diagnosis of petit mal was made. Serologic tests for syphilis gave strongly positive reactions, and she received twelve injections of arsphenamine and twelve of a bismuth compound. She failed to return for further therapy until April 20, 1939, when she came in complaining of blue mottling of her skin.

On the flexor surface of the forearms and to a lesser degree on the trunk and the lower extremities there is a coarse network of purplish blue mottling. The eruption seems to follow the course of underlying blood vessels.

Neurologic examination gave negative results. Serologic tests of the blood and spinal fluid for syphilis now give negative reactions.

DISCUSSION

Dr. H. N. Cole: This patient, although she shows no evidence of syphilis, has the disease. Ehrmann has called attention to certain conditions with syphilis as a background. About twenty years ago I saw a German boy with early syphilis. He was given treatment for about two years. At that time continuous therapy was not in use, and he went back to Germany. He stayed there for about four years. On his return to the United States he came in to see me because of a peculiar eruption on his body. He had one of the most extensive eruptions of livedo racemosa I have ever seen. I looked him over carefully for evidence of syphilis. The spinal fluid was normal, but I interpreted the process as a relapse. I gave treatment for a short time, and he disappeared from observation. I have not seen him since.

Dr. Gerald Anthony DeOreo: On looking back I found that 35 cases of one type or another of livedo racemosa have been reported in the Archives of Dermatology and Syphilology. In only 3 of these, however, was the condition attributed to syphilis. In 2 cases there was a positive Wassermann reaction, but the condition was not ascribed to syphilis. In the other cases tuberculosis and rheumatism played a part. There was disseminated lupus erythematosus in 2 cases.

Trophic Ulcers of the Face and Neck Due to Syringobulbia. Presented by Dr. W. F. Schwartz.

R. E., a woman aged 40, is presented from the department of dermatology and syphilology, City Hospital. She has complained of numbness of the left side of the face for a little more than five years. Shortly after the onset she burned herself with a heat lamp in the region of the ear. Since then there have been recurrent superficial ulcers above and behind the left ear. These healed spontaneously, leaving an atrophic scar, only to be followed by ulceration. About six months ago the numbness in the face progressed down to the left side of the neck, the left shoulder and eventually the right shoulder and the radial aspects of both arms and hands. The recurrent superficial ulcerative lesions have extended to involve the left side of the face and neck.

Trophic ulcers of the face and neck due to syringobulbia.

The area of anesthesia corresponds to the distribution of the sensory part of the fifth cranial nerve, especially the maxillary and mandibular branches, and also to that of the cervical nerves down to the fourth. There is dissociation of sensation, touch being better preserved than pain and temperature. The sensory defect is now spread bilaterally over both shoulders and down the radial surfaces of both arms and is associated with early interosseous atrophy. The tongue shows some atrophy. The pharyngeal reflexes are sluggish. There is rotary nystagmus to the left. There is no muscle "tendon" reflex change.

On the skin there are confluent atrophic and hyperemic scars above and behind the left ear as well as on the lower part of the left cheek and the side of the neck. These are the results of the recently healed ulcers. The left external ear shows atrophy. The crusted ulcers before healing occurred are shown in the accompanying illustration.

The hemogram revealed moderate secondary anemia. Serologic tests for syphilis gave negative reactions. The spinal fluid was normal.

Healing was rapid after the use of an ointment containing Aloe vera.

DISCUSSION

DR. W. F. SCHWARTZ: One of the first reasons for presenting this patient is that it is unusual to see trophic ulcers in this region. The most important reason for showing her is that there was considerable difficulty in recognizing the condition as trophic ulcer in its early stages. There would be bizarrely shaped superficial ulcers above and behind the ear on one visit, and on another these would be healed and there would be some in a different region. Dermatitis factitia was the diagnosis made at that time. It was not until the disease had extended to the front of the ear, the patient complained bitterly of numbness of the face and atrophy of the ear was noticed that a lesion of the central nervous system was suspected.

DR. JOHN E. RAUSCHKOLB: It is interesting that neurologists see such conditions frequently and recognize them readily. I have labored with this patient for two years before I arrived at a diagnosis, and then I did so only with the aid of neurologic consultation.

Facial Paralysis Due to Early Syphilis of the Central Nervous System; Granuloma Inguinale. Presented by DR. W. F. SCHWARTZ.

J. M., a Negro aged 25, is presented from the department of dermatology and syphilology, Cleveland City Hospital. Nine months ago he had a penile sore which was diagnosed as primary syphilis. He received no treatment at that time. Three months later he suddenly had crossed hemiparesis, of the left side of the face and of the right arm and leg. The paralysis of the extremities lasted about one week, but the facial paralysis did not improve. Two months ago the patient was admitted to the City Hospital because of another penile sore, which had been present a little more than one month. This has been diagnosed as granuloma inguinale. In the past two months three injections of a soluble bismuth preparation and thirteen of mapharsen have been given. The facial paralysis has improved considerably.

At present the patient presents a granulomatous ulcer on the shaft of the penis, from which Donovan bodies have been demonstrated. At the time of his admission to the hospital there was decided paresis of the facial muscles on the left as well as of the muscles of the forehead on the same side. There was no evidence of involvement of any of the cranial nerves other than the seventh. The muscle tone, the deep and superficial reflexes and the sensory changes of the extremities were essentially normal and equal. The skin was free of eruption.

Serologic tests for syphilis gave strongly positive reactions. The Wassermann reaction of the spinal fluid was 1 plus in 0.5 cc. and 4 plus in 1 cc. The cell count was 5 per cubic millimeter, and the mastic curve, 2210000000. The Pandy reaction was 1 plus.

DISCUSSION

DR. H. N. COLE: There are many cases of Bell's palsy not related to syphilis, but one should keep in mind the possibility of Bell's palsy of syphilitic origin. Some years ago there were 2 patients in the hospital at the same time with a syphilitic type of Bell's palsy. Since then I have not seen any until I saw this Negro with early syphilitic paraplegia and Bell's palsy. The disease does not always respond readily. It is much like other types of Bell's palsy in that respect.

Juvenile Tabes Dorsalis. Presented by DR. W. F. SCHWARTZ.

B. V., a girl aged 16, is presented from the department of dermatology and syphilology, City Hospital. In December 1934 she first sought treatment at the Lakeside Hospital for occasional headaches and failing vision. Serologic tests of

the blood gave strongly positive reactions, and the Wassermann reaction of the spinal fluid was also positive, and with the mastic curve was 21110000000. The patient had had no previous therapy for syphilis. Her father and two siblings, aged 13 and 22, have been examined and showed no physical or laboratory signs of syphilis. Two other siblings, aged 25 and 28, have not been examined. The mother, who is 51, has syphilis but shows no physical or laboratory signs of involvement of the central nervous system. There have been no miscarriages.

During the past four years the patient has received the following medicaments: acetarsone for seven months (Jan. 11 to Aug. 16, 1935); neoarsphenamine, twenty-eight injections; bismuth subsalicylate, eighty-two injections, and pyrifer (a non-specific protein mixture of extracts of fever-producing bacteria from certain non-pathogenic stocks), three courses, with a total of thirty-six treatments.

The patient is well developed and well nourished, with no structural stigmas of congenital syphilis. An intelligence test indicated normal average intelligence. The pupils were dilated, irregular and fixed to light. The deep and superficial reflexes of the upper extremities were normal. All deep reflexes of the lower extremities were absent, but there was no change in the superficial reflexes. The sense of position was slightly impaired, and there was slight ataxia, but a Romberg sign could not be demonstrated. Consultation with physicians of the genitourinary department resulted in a tentative diagnosis of tabetic bladder. There has been no incontinence.

Serologic tests of the blood and spinal fluid for syphilis gave negative results at this time.

DISCUSSION

DR. H. N. COLE: I think there is a tendency to take the position that one cannot expect much improvement from treatment of juvenile tabes and dementia paralytica. Some patients, however, improve remarkably under antisyphilitic therapy, particularly fever therapy. I do not think it makes a great deal of difference whether one uses artificial fever therapy, malaria or a bacterial foreign protein preparation.

DR. C. L. CUMMER: I wish to support Dr. Cole's statement. I remember a boy who had well marked juvenile tabes before the introduction of fever therapy. He is now married, the father of two children and perfectly normal. He looked hopeless about ten years ago.

DR. W. F. SCHWARTZ: Such cases are distinctly uncommon. So far as I know, this patient is the only one with juvenile tabes registered in the dermatologic clinic at the City Hospital. The symptoms of juvenile tabes dorsalis are not as severe as those of the acquired form. Even in cases in which there are full-blown physical signs that the disease has affected the vital organs, such as cord bladder, there are very few symptoms.

DR. E. W. NETHERTON: It is interesting to note that this child shows syphilis and is between two other children who show no signs. We do not know about the two oldest children, but this would be a rather high incidence of nonsyphilitic babies from an untreated syphilitic mother. I wonder whether the mother was treated during any of her pregnancies.

DR. W. F. SCHWARTZ: When the patient reported at the Lakeside Hospital in 1935, syphilis in the family was discovered for the first time. The mother has latent syphilis without involvement of the central nervous system.

Mycosis Fungoides. Presented by DR. W. F. SCHWARTZ.

E. D., a man aged 65, was first seen at the City Hospital one year ago, at which time he complained of a painless mass protruding from the skin of the right groin, which he stated had been developing for three or four months. He also had a generalized exfoliating dermatitis which had developed gradually over twenty years and which he stated had been called "psoriasis." There had never been any pruritus. A few small soft flat nodules were seen on the abdomen and

in the axillary region. The mass in the groin, as well as these nodules, resolved rapidly under the influence of roentgen therapy. During the past year similar soft nodules, either discrete or arranged in circular groups, have appeared on the trunk, and these have likewise responded rapidly to four or five roentgen ray treatments (80 r each). Pruritus has now become a prominent symptom. The exfoliation has become possibly a little more extensive.

Except for the palms and soles, almost all surfaces of the body are affected by a brownish red, slightly scaling dermatitis. It is universal except for several areas where it is interrupted by configurate patches of normal skin. There are a few soft flat nodules scattered throughout the eruption.

The liver, spleen and lymph nodes are not enlarged. Roentgen examination of the chest showed no evidence of parenchymatous infiltration in the lung fields or enlargement of the mediastinal lymph nodes. The hemogram was normal, and serologic tests for syphilis gave negative reactions.

Six specimens were removed for histologic examination, one from the sternal bone marrow and five from the skin. The sternal bone marrow was normal. Tissue taken from one of the soft nodules as well as that taken from a non-infiltrated scaling patch showed no evidence of lymphoblastoma and was reported by the pathologists as showing only chronic inflammation. Sections of tissue taken from the mass in the groin were reported as lymphoblastoma of the skin. The tissue from the tumor in the groin showed the epithelium to be the seat of mild parakeratosis and varying degrees of acanthosis. The epithelial pegs were elongated, slender and irregular. The cells composing some of their tips were separated by edema and cells of the type to be described as occurring in the corium, so that the basal layer of a considerable portion was fuzzy and extremely irregular. There was diffuse cellular infiltration in the corium, extremely well delimited to the papillary and superficial portions of the subpapillary layer. The cells comprising the exudate consisted chiefly of lymphocytes, with smaller numbers of large mononuclear cells, eosinophils and a few cells which could not be identified. One or two mitoses were seen, but no giant cells were present.

Tissue removed recently from one of the cutaneous nodules showed that the squamous epithelium was absent in most places. The remaining fragments showed severe inflammatory hyperplasia. The surface of the tissue was necrotic, and an acute purulent exudate was present in this region. In the underlying tissue severe inflammatory changes were also present, but these were more subacute, as was evidenced by numerous eosinophils. Granulation tissue was present in places. In addition, there were numerous large, irregular cells arranged in a diffuse manner. These cells had large, vesicular and in general round nuclei with one or more prominent nucleoli. A few of these cells were multinucleated. Mitotic figures were fairly frequent. Many of the cells contained clear vacuoles in their cytoplasm. There were no definite structural formations. A stain for mucin gave negative results. A stain for reticulum gave positive results.

DISCUSSION

DR. H. A. BRUNSTING: I should like to ask about the therapy.

DR. H. N. COLE: Lomholt has reported some rather favorable results from the use of chaulmoogra oil for mycosis fungoides. At the Montreal meeting of the American Dermatological Association, Dr. Hiram C. Miller mentioned a case of mycosis fungoides in which he gave fever therapy and obtained a severe response. It almost killed the patient, but the mycosis fungoides disappeared. That, of course, is an isolated instance.

DR. W. F. SCHWARTZ: I have considered fever therapy but was not particularly impressed by the isolated report in the literature of a single case in which use of the Kettering hypertherm produced temporary benefit.

DR. E. W. NETHERTON: I should like to ask Dr. Work whether from the standpoint of the pathologist he would say this is Hodgkin's disease.

DR. JOHN WORK (by invitation): The pathologic concept of mycosis fungoides differs from the clinical concept. My experience has been that conditions which are typical clinically of mycosis fungoides may be any of a number of lymphoblastomas. Some are Hodgkin's disease; some, sarcoma. I think the condition in the present case must be regarded as a form of Hodgkin's disease or reticulum cell sarcoma. One sees Hodgkin's disease affecting the liver, spleen or lymph nodes. I am not going so far as to call this definitely Hodgkin's disease, but reticulum cells and many other abnormal cells are present. There are a few giant cells similar to Reed-Sternberg cells. The mere fact that one calls the condition Hodgkin's disease does not mean that it is not mycosis fungoides. In the light of my experience and the pathologic experience of others, I think mycosis fungoides is a characteristic type of cutaneous disease that may be due to any one or a number of lymphoblastomas. In some cases it may be caused by reticulum cell sarcoma and in some by Hodgkin's disease.

NEW YORK ACADEMY OF MEDICINE, SECTION OF DERMATOLOGY AND SYPHILIS

EUGENE F. TRAUB, M.D., *Chairman*

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April 28, 1939

Symposium on Syphilis

Recent Periostitis Developing During Treatment of Late Syphilis. Iridocyclitis (Old) with Secondary Glaucoma. Presented by DR. LEO SPIEGEL.

E. S., a woman aged 38, presented from Bellevue Hospital, has an infection of unknown duration. It was first discovered on Jan. 24, 1938, when the patient came to Bellevue Hospital with an active iridocyclitis of the left eye believed to be of syphilitic origin when examined in the ophthalmic department. On January 25 the Wassermann reaction was 4 plus. The patient had no treatment prior to this time. Since that day she has received thirty injections of a bismuth preparation and twenty-five injections of arsenicals (sixteen of arsphenamine and nineteen of mapharsen) in the syphilis clinic. The iridocyclitis responded promptly to antisyphilitic treatment.

On Feb. 10, 1939, while under treatment, the patient began to complain of an aching pain in both shins, worse at night and in the early morning. Exercise did not make it worse. Repeated examinations in the clinic revealed no tenderness. Roentgenograms of the legs showed moderate periosteal thickening of the lateral aspects of both tibias, suggestive of syphilitic periostitis. The patient was receiving mapharsen at the time of the onset of her pains. Owing to severe gastrointestinal reactions, the doses of arsphenamine were reduced from 0.3 Gm. to 0.2 Gm., early in the course of treatment. The highest dose of mapharsen tolerated was 0.03 Gm.

The Wassermann reaction of the blood has been 4 plus at all times since Jan. 25, 1938. The results of tests of the spinal fluid on February 15 were normal. Roentgenograms of the heart and the aorta were normal. Roentgenograms of the long bones are presented for inspection.

The case is presented in order to find the cause of the periostitis.

DISCUSSION

DR. EVAN W. THOMAS (by invitation): I have never encountered a case like this. I believe the condition is late syphilis. In every case of late syphilis of the bones that I have observed, however, there has been an osteitis along with the periostitis.

DR. E. W. ABRAMOWITZ: Syphilis of the eye and bone is not uncommon in Negroes. No doubt this patient has some periosteal involvement. When treating a patient with medicaments containing bismuth, unusual complications sometimes develop. Bismuth rheumatism and deposits of bismuth in the bones may occur. In cases in which the bone symptoms do not seem to respond to the bismuth preparation used, a complete change in treatment should be made. Bismuth should be discarded and mercury given by injection. If the patient is intolerant to arsphenamine, it might be omitted; or perhaps a different type of arsenical might be used, a pentavalent rather than a trivalent arsenic compound. The point I am interested in is whether Dr. Spiegel can rule out a possible deleterious effect on the bones from the bismuth itself.

DR. ISADORE ROSEN: I wonder whether this patient received any iodides during the rest periods. It might be advisable to stop the intravenous and intramuscular medication for the present and administer iodides in medium-sized doses. The administration should be followed with a roentgenogram, to show the effect.

DR. LEO SPIEGEL: I have observed patients with syphilis who had severe pains in the joints and muscles after long courses of treatment with a bismuth preparation. I agree with Dr. Rosen about administering iodides, but before that I should give the patient three or four injections of sodium thiosulfate and nothing else, to see if the pains disappear. The pains may be due to the continued use of bismuth although the roentgenograms show evidence of periostitis due to syphilis.

DR. EVAN W. THOMAS (by invitation): Since the roentgenograms have been examined, which was only about two weeks ago, all treatment has been stopped. The patient had had alternate courses of treatment with a bismuth preparation and with mapharsen, beginning with the bismuth compound. I ordered mercuric succinimide in daily injections, but she refused to come in more than once a week. I doubt if she is intelligent enough to take mercury inunctions properly. I think that stopping arsenical treatment for the present and giving only iodides will be helpful, or perhaps mercury inunctions could be tried in spite of her lack of good cooperation.

Osteoperiostitis of the Femur. Presented by DR. LEO SPIEGEL.

F. F., a woman aged 40, with a syphilitic infection of about seven years' duration, is presented from Bellevue Hospital. A routine Wassermann test on Dec. 20, 1938, gave a 4 plus reaction. For four years before this the patient had been complaining of pain in the right thigh, which was worse at night. She had had no treatment before December 20, when she was admitted to the syphilis clinic.

Examination of the spinal fluid on Jan. 11, 1939, gave negative results. Roentgenograms of the heart and the aorta on January 18 were normal. Roentgenograms of the long bones on January 11 showed osteoperiostitis of the medial aspect of the proximal half of the right femur.

Meningomyelitis Syphilitica with Muscular Atrophy. Presented by DR. LOUIS CHARGIN.

J. M., an Austrian aged 26, is presented from the Central Social Hygiene Clinic of the Department of Health, with Dr. Luis Perelman. The patient says that he has not had syphilis. In February 1938 he noticed progressive weakness and clumsiness of the hands, wasting of the muscles of all four extremities and numbness of the hands and feet. A diagnosis of progressive muscular atrophy was made by a neurologist. For a time the patient was treated with electrotherapy but without benefit. He was admitted to Mount Sinai Hospital on July 22, where examination revealed bilateral wrist drop, foot drop, definite atrophy of the muscles of the extremities, profound weakness of the distal muscles of the extremities and complete absence of deep reflexes except for the pectoral muscles. Vibratory sensation was absent from the iliac crests down, and there was diminished sensation of pain, touch and temperature over the fourth lumbar

and the first sacral segment bilaterally. Lumbar puncture showed a partial block, Examination of the spinal fluid showed 135 mononuclear cells and a total protein of 88. The Wassermann reaction of the spinal fluid was 4 plus, and the colloidal gold curve was 1122211000. The Wassermann reaction of the blood was also 4 plus. The patient was discharged from Mount Sinai Hospital on September 2, unimproved.

The patient was next admitted to the Meinhardt Clinic on October 20, where examination showed the motor system to be as previously described, the Romberg reaction positive, the deep reflexes absent and the sensory system as previously described, with, in addition, hypalgesia to pinprick on the ulnar aspects of both upper extremities. The Biernacki and Abadie signs were positive. Examination showed no evidence of abnormality of the cranial nerves except that the pupils were unequal, the right being larger than the left. The libido is decreased, and the patient has erotic dreams and disturbances of the bladder.

There is definite proof of involvement of the posterior column and degeneration of the anterior horn cells. A diagnosis of syphilitic meningomyelitis appears to be justified. To date the patient has received ten injections of silver arsphenamine and fourteen injections of a bismuth preparation, with no apparent improvement.

DISCUSSION

DR. LEO SPIEGEL: I should like Dr. Perelman to tell whether the patient has improved.

DR. LUIS PERELMAN (by invitation): The therapy has not been effective. The man consulted a physician because he had had an accident, after which a weakness of the arms developed. The presenting symptom was weakness of the arms, with wasting away of the muscles. He was taken to a specialist, and a diagnosis was made of progressive muscular atrophy. I presume that at that time he had no sensory changes, but they are evident now. His symptoms then were due to lesions resulting from degeneration of the anterior horn cells. This is not a case of tabes. The subjective symptoms oscillate, but objectively the patient does not appear improved. I believe that the pathologic process is vascular and that the lesions will eventually lead to occlusion of the vessels. In that case the changes will be irreversible and the result of treatment questionable. All that can be hoped for is an arrest in the progress of the disease. He has enough cells still intact so that he can use his extremities to the extent he does. With physical therapy these muscles may be saved, and if the antisyphilitic treatment is continued, the process may not progress. The textbooks describe good responses to treatment in such cases. The therapy was started a little late, and that may be the reason why it has been ineffectual. I have never encountered a case like this and therefore cannot given an opinion as to what the results might have been had the therapy been started earlier.

At a conference of neurologists where this patient was presented, there were some suggestions as to therapy. Attention was drawn to the fact that many muscles are still intact. There was not much hope expressed for the possibility of reversal of the syndrome. The active pathologic change is not likely to be reversed. The patient will be referred to the Neurological Institute of New York where the physicians may have some further ideas as to therapy. The suggestion of fever therapy will have to be deferred, because the patient's defenses are at a low ebb and the reaction would be too severe.

DR. LEO SPIEGEL: When was the spinal fluid examined?

DR. LUIS PERELMAN (by invitation): In August 1938.

DR. LEO SPIEGEL: That was a long time ago. While this man has been treated with silver arsphenamine, he also should have been given sodium iodide intravenously in large doses. An active pathologic process is shown by the increased number of cells in the spinal fluid. The spinal fluid should be examined every three months, and if there is no favorable response in six months following

the combined courses of arsenicals, bismuth preparations and sodium iodide, and if the patient is otherwise in good physical condition, fever therapy should be tried.

DR. LUIS PERELMAN (by invitation): I should like to be optimistic, but I have seen the patient once a week, and I believe his condition is getting worse. I believe the therapy has been adequate. He has been given the routine therapy that the physicians of the department of health prescribe in cases of neurosyphilis. Outside of a hospital I believe nothing more could have been done without exposing him to danger. He has had rather severe reactions at times to silver arsphenamine. The examination of the spinal fluid was made six months ago, but it was not repeated because the man is weak and is an invalid most of the time. Plans are being made to have him hospitalized as soon as possible.

Tertiary Syphilis: Transverse Myelitis Following Administration of a Bismuth Compound. Presented by DR. A. BENSON CANNON.

A. DeG., an Italian aged 41, is presented from Vanderbilt Clinic. He states that he had gonorrhea and a questionable chancre in 1919. Four intravenous injections were given at that time. No intramuscular injections were given. He had no further treatment until he was admitted to Vanderbilt Clinic in April 1931. On admission the Wassermann reaction of the blood was 4 plus. He complained of severe continuous and throbbing headaches, located mainly in the right parietal region. Examination showed that the pupils reacted to light and in accommodation but the ankle and knee jerks were overactive; otherwise the results of the examination were negative. Treatment was begun with the administration of bismuth preparations, and two injections were given, on April 30 and on May 7, 1931. Following the second injection a transverse myelitis with complete paralysis of the lower extremities developed. The patient was admitted to the New York City Hospital and there regained partial use of his legs. He is now able to walk with the help of a cane but has not been able to return to his former occupation of taxi driver. The Wassermann reaction of the spinal fluid has remained 4 plus since the first examination in 1931. The Wassermann reaction of the blood is now 2 plus with an alcoholic antigen and 3 plus with a cholesterolized antigen. Treatment has consisted of one hundred and twenty injections of a bismuth preparation, fifty injections of old arsphenamine, twenty injections of tryparsamide and sixteen Swift-Ellis injections.

Examination at the present time shows equal and active pupils, slight leukoplakia of the mucous membrane opposite the last upper molar on the right side, hyperactive knee jerks and ankle jerks and a normal heart. The lungs and abdomen are normal.

The case is of particular interest because of the transverse myelitis which followed only two injections of a bismuth preparation.

DISCUSSION

DR. HERMAN GOODMAN: Were there any clinical or serologic observations prior to the injection of the bismuth preparation which would lead one to suspect the possibility of injury of the nervous system?

DR. EVAN W. THOMAS (by invitation): What is the nature of the transverse myelitis? Is it due to an inflammatory lesion of the cord or to a vascular condition?

DR. FRANK E. CROSS (by invitation): I do not believe the bismuth compound had anything to do with the transverse myelitis. I think the development of the condition just after the injections was a coincidence.

DR. L. C. RUBIN (by invitation): Were there any sensory changes? Did the patient have any trouble with the sphincters of the bladder or rectum? What is the diagnosis of transverse myelitis based on?

DR. HENRY D. NILES: I also question the diagnosis. There is no statement in the history about a colloidal gold test or about testing for ankle clonus or for the Babinski or Romberg sign. I think these are all necessary.

DR. LUIS PERELMAN (by invitation): I should not venture a diagnosis on the basis of the summary on the history card. I should like to know if the patient has any pathologic reflexes or an upper motor neuron or a lower motor neuron syndrome.

DR. JAMES L. MILLER: On admission the patient had a positive Wassermann reaction of the blood and of the spinal fluid. The transverse myelitis was probably due to the bismuth administered, but it was a syphilitic myelitis, precipitated by the bismuth in the same manner as a Herxheimer reaction.

Tertiary Syphilis: Aneurysm of the Ascending Portion of the Aorta.
Presented by DR. JAMES L. MILLER.

Mrs. L. J., a Negress aged 33, was admitted to Presbyterian Hospital on June 4, 1935, complaining of pain and "thumping" in the right side of the chest for two months. These symptoms began after a severe cold. The patient also complained of cough, anorexia and the loss of 10 pounds (4.5 Kg.). She had nocturnal dyspnea but no edema of the ankles. Physical examination showed a slight tracheal tug, a difference in blood pressure between the two arms (150 systolic and 90 diastolic on the right side and 120 systolic and 90 diastolic on the left side) and an expansile pulsating mass at the right second interspace. A harsh systolic murmur was heard at the apex and the aortic area. Roentgenograms and fluoroscopic examination showed a saccular aneurysm of the ascending portion of the aorta. The Wassermann reaction of the blood was 4 plus.

The patient was given fifteen injections of a bismuth preparation intramuscularly and iodides orally. The aneurysm was wired by Dr. Blakemore in the Presbyterian Hospital on two occasions in 1935. A small portion of the aneurysm still remained active, and this was rewired in 1936. The patient has received about seventy injections of a bismuth preparation intramuscularly, accompanied by the iodides, in the four years since the aneurysm was first wired. No arsphenamine has been given. The patient has remained free, as determined by physical and roentgenographic examination. The aneurysm has remained stationary in size, and no new aneurysms have developed. The Wassermann reaction of the blood is now negative.

DISCUSSION

DR. JAMES L. MILLER: The patient has had no pain or edema of the ankles or severe dyspnea. She is able to return to work and does not feel that she has any particular trouble. The case demonstrates how easily the diagnosis might have been made earlier. The condition of her husband, who had had a positive Wassermann reaction, had been diagnosed as syphilis seven years before the patient came to the hospital. She had had three miscarriages, at seven, at five and at three months, and the diagnosis of syphilis might have been suspected then.

Tertiary Syphilis: Aneurysm of the Ascending Portion of the Aorta.
Presented by DR. LESLIE P. BARKER.

Mrs. E. R., a Negress aged 46, is presented from Vanderbilt Clinic. She has had increasing dyspnea for the past twenty-six years, but her condition has remained about the same for the past six years, during which time she has been unable to climb stairs or do any manual labor. She was told in 1923 at St. Luke's Hospital that she had syphilis and received about twenty intravenous injections and forty intramuscular injections at that time. She was admitted to Vanderbilt Clinic in 1931, complaining of dyspnea, cough and substernal pain. Examination revealed an aneurysm of the ascending portion of the aorta, about 8 cm. in diameter. She was given antisyphilitic treatment with bismuth preparations and iodides, and after twenty injections of a bismuth compound small doses of arsphenamine were given. Repeated roentgenograms showed enlargement of the aneurysm, and there was a continued increase in symptoms. The aneurysm was wired by Dr. Blakemore in 1935, and within ten months all the substernal pain had disappeared, the cough had improved and the patient was able to walk eight

blocks without exhaustion, whereas previously she had been able to walk only two blocks. She has continued to improve since that time.

The Wassermann reaction of the blood and the observations on the spinal fluid have been normal since she was admitted to Vanderbilt Clinic.

DISCUSSION

DR. EVAN W. THOMAS (by invitation): In what percentage of cases of this kind does surgical intervention fail to relieve pain or other symptoms?

DR. LESLIE P. BARKER: Success of the operation depends on the type of aneurysm treated. The saccular type with a very small mouth is the ideal type for wiring, because the flow of blood in the sac is very slow, and it is easier in this type to obtain a clot large enough to obliterate the aneurysmal sac than in the fusiform type, in which the flow of blood is so rapid that it is difficult to obtain clotting.

DR. HERMAN GOODMAN: What is the fatality of this operation?

DR. JAMES L. MILLER: There have been about 19 patients, 5 or 6 of whom died subsequent to the operation. However, the condition was far advanced in them, and the operation was performed in the days when the technic was first introduced. There is a certain amount of reaction as a result of the heating of the wire. That reaction is considered good, however. There is a certain amount of damage to the surrounding wall, but that can now be controlled, and a certain amount is considered a good thing, because fibrosis occurs afterward. At first, however, the operation apparently resulted in several untoward results, with death occurring in the first five days after operation. The technic has been improved now. Dr. Blakemore has recently reported his results (Blakemore, A. H., and King, B. G.: Electrothermic Coagulation of Aortic Aneurysms, *J. A. M. A.* **111**: 1821 [Nov. 12] 1938).

Aortitis; Aortic Regurgitation; Aneurysm of the Thoracic Aorta. Presented by DR. LOUIS CHARGIN.

B. J., a Negro aged 59, is presented from the Central Social Hygiene Clinic of the Department of Health, with Dr. L. C. Robin. The patient had a penile sore thirty-four years ago which was treated by chemical cauterization. He says that he did not have an eruption. A routine serologic test a year later gave a negative result. About five years ago the patient began to complain of pain in the lower part of the left side of the chest, in the axillary line, accompanied by dyspnea. These attacks increased in frequency. Three years ago the Wassermann reaction of the blood was 4 plus. He received antisyphilitic treatment, consisting of eight injections in the arm and twenty-six in the hip during 1936 and 1937. The pain, however, has not been relieved and is practically always present. There are moderate dyspnea and palpitation on exertion. Since 1937 the patient has been receiving injections of a bismuth preparation and of potassium iodide.

Physical examination shows a well developed but thin elderly man. The heart is enlarged at the apex, downward to the sixth left interspace and outward to the anterior axillary line. There are no thrills or shocks. A soft diastolic murmur is heard best over the aortic area to the right of the sternum at the second interspace. A double murmur is heard at the apex. The pulse rate is regular. The blood pressure is 150 systolic and 90 diastolic in the right arm and 140 systolic and 90 diastolic in the left arm. The pupils are equal, and there is no tracheal tug. Examination of the lungs shows a palm-sized area of dulness with suppressed breath sounds posterior to the left of the spine at the level of the angle of the scapula. The liver is palpable 2 fingerbreadths below the costal margin. There is bilateral pretibial edema, more evident on the right side.

Fluoroscopic and roentgenographic examinations showed the heart to be enlarged in the transverse and oblique diameters. In the left anterior oblique

view the cardiac shadow extended beyond that of the spine, indicating left ventricular enlargement. The myocardial tone was impaired. The aorta was diffusely dilated, as manifested by obliteration of the right aortic distance and by broadening of the supracardiac shadow to the left. In addition, there was a moderate fusiform dilatation of the descending aorta, and in the left anterior oblique portion there was noted, arising from the posterior wall of the midthoracic aorta, a saccular aneurysm the size of a tangerine. Pulsation in the latter was not increased.

DISCUSSION

DR. L. C. RUBIN (by invitation): The patient is doing well under treatment with bismuth preparations and potassium iodide in courses, with rest periods in between. He is still working, but at a job at which he sits down. He was formerly a laborer.

DR. E. W. ABRAMOWITZ: Every once in a while a roentgen examination shows sacculation of the arch or of another portion of the aorta, while the patient has practically no symptoms of aortic involvement. There was a patient recently at the Gouverneur Hospital with a great enlargement of the descending portion of the arch of the aorta. He had no pain and had been taking treatment at the syphilis clinic with no ill effects. He was admitted to the hospital for some other condition. Such patients apparently can carry on light work even though their illness is considered serious.

DR. I. ROSEN: These 3 cases of aortic aneurysm should impress on the physician who treats syphilis the importance of early roentgen examination of all patients with the disease. In the treatment of aortic aneurysm it is important to outline a form of therapy which is mild and is carried on interruptedly over a long period. I have made it a plan not to give these patients any arsenicals intravenously, and I am satisfied with giving a bismuth preparation or mercury intramuscularly and iodides during the rest periods.

DR. L. C. RUBIN (by invitation): We make routine fluoroscopic examinations of all the syphilitic patients at the clinic. I think one point that should be mentioned in the routine treatment of these patients is the necessary reduction of their activity, which is as important as the administration of drugs.

Erb's Spastic Paraplegia; Primary of the Optic Nerve. Presented by DR. LEO SPIEGEL.

G. S., a man aged 50, is presented from Bellevue Hospital with a syphilitic infection of unknown duration. The patient first noted slight difficulty in walking in 1931, at which time a positive Wassermann reaction of the blood was observed at Bellevue Hospital. However, the patient did not report for antisyphilitic treatment. In November 1938 he began to notice stiffness in the muscles of the right leg, described as a drawing feeling in the muscles. This gradually became worse and spread to the left leg. He came to Bellevue Hospital on December 31 because of a spastic gait. He also stated that he had first noticed poor vision in the left eye about Dec. 1, 1938.

Physical examination showed that the pupils were equal and fairly regular and reacted to light and in accommodation. Both optic disks were slightly grayish, and the outer temporal margin of the left disk showed slight pallor. Sensation (touch, temperature and vibration) was normal. The biceps and triceps jerks were slightly hyperactive. The ankle and knee jerks were strongly hyperactive, the right being greater than the left. There were bilateral ankle clonus and patellar clonus on the right. There was a positive Babinski sign on both sides. Abdominal and cremasteric reflexes were present. The abductor muscles of both legs were very weak, the right being weaker than the left. The gait was spastic, more on the right side than on the left. On Feb. 24, 1939, the ocular examination showed no central scotoma. The color sense was good with artificial light. The

perimetric fields showed interesting quadrant defects involving the upper nasal portion of the right retina and the lower and upper temporal portions of the left retina.

On Dec. 27, 1938, the Wassermann reaction of the blood was 4 plus. On Jan. 30, 1939, examination of the spinal fluid showed the Wassermann reaction to be 4 plus with 1 cc. and 0.5 cc. and plus-minus with 0.1 cc. The cell count was 0, there was no globulin and the colloidal gold curve was 0000000000. Roentgenograms of the heart and aorta were normal.

DISCUSSION

DR. EVAN W. THOMAS (by invitation): I never expected to encounter such an unusual case. Spastic paraplegia is listed in the diagnostic index but is rarely seen. I think this patient presents about as near the textbook picture of this condition as one can get, both in onset and in physical signs. Whether the condition is due to syphilis or not I leave to the members. It is certainly included among the syphilitic manifestations in the spinal cord. A few cases in which autopsy has been performed are described in the literature. The same type of pathologic changes are described in the lateral pyramidal tracts that are seen in the dorsal columns in tabes dorsalis. The changes have been ascribed to syphilis because there has been associated syphilis in some of these cases; but syphilis has not been present in all instances. There have been 1 or 2 cases in which autopsy was performed in which a positive Wassermann reaction was not obtained and in which the results of the examination of the spinal fluid were negative. This man's condition came on gradually. When seen in the clinic he had a spastic gait which could be differentiated from an ataxic gait. The abductor muscles in spastic paraplegia are always weaker than the adductors. He has a bilateral Babinski sign and bilateral ankle clonus, with patellar clonus on the right. He has, in addition, primary atrophy of the optic nerve, which has never been described in association with spastic paraplegia, so far as I have been able to find out in my perusal of the literature. When the patient was first examined, on Jan. 23, 1939, both disks were grayish, not the typical white disks of primary atrophy of the optic nerve. I was slightly skeptical as to whether he had true primary atrophy. He has been seen by several physicians, all of whom have come to the conclusion that the condition is a definite primary atrophy with unusual visual fields. The vision is worse in the left eye than in the right. He has been under treatment only since February 1, and I cannot say that there has been any improvement one way or the other. He says he is better. He received a bismuth preparation and then pentavalent arsenic. I have come to the conclusion that in many of these patients there is a tonic effect from the pentavalent arsenicals. The patient says he feels better, yet there is no improvement in the condition of the spinal fluid or it may even be worse. I should like to hear a discussion on the value of pentavalent arsenicals in syphilis and especially in tabes dorsalis, because I wonder if tabes dorsalis is not a meningovascular syphilis due to involvement of the meninges and vessels at the roots and if it is not a very different thing from the parenchymatous form seen in dementia paralytica. I offer that as a possibility. From a study of our charts I can say that the pentavalent arsenicals are of dubious value in the vascular and meningovascular types of syphilis, but I believe they are of value in the parenchymatous type of syphilis of the central nervous system known as dementia paralytica.

DR. LEO SPIEGEL: When tabes dorsalis is observed early in a patient and the various tests on the spinal fluid show active inflammatory reactions, it is my custom to use at first the trivalent arsenicals. The inflammatory reactions in the spinal fluid in these cases show an increased cell count, a definite increase in globulin and protein and various degrees of positivity with a quantitative Wassermann test. Unfortunately, tests for protein and globulin are not done routinely in examining the spinal fluid. The so-called tests for globulin, such as the Pandy, the Nonne-Apelt and the Noguchi, are indefinite and inaccurate and give no information as to the extent of the pathologic process. The proteins should be

tested for by accurate methods, such as the Exton-Rose test, and the turbidities read with suitable instruments. Of the trivalent arsenicals, I, as well as many other observers, prefer silver arsphenamine. This preparation has a somewhat crystalloid structure and supposedly penetrates the meningovascular barrier more readily that the other trivalent arsenicals. It has therefore been my custom to start treatment in these cases, as well as in cases of meningovascular syphilis, with silver arsphenamine and then with old arsphenamine, giving two courses, one of each. Courses of intramuscular injection of bismuth preparations and intravenous injections of sodium iodide are given between the injections of arsphenamine. According to some observers (Moore and others), sodium iodide also penetrates the meninges more readily than potassium iodide when given by mouth. After the aforementioned therapy, I invariably use the pentavalent arsenicals. This remedy has been used for the past four years with gratifying results in many instances. In the cases of so-called "burnt out" tabes dorsalis, when the tests of the spinal fluid are negative, no form of antisyphilitic therapy is of benefit. Supportive tonic treatment is then of some help, as the patients are often below par and undernourished.

Dr. Luis Perelman (by invitation): I should like to ask Dr. Thomas what the status of the upper extremities is and if any other cranial nerves are involved. Are there any sensory changes? What are the serologic changes of the spinal fluid?

Dr. Evan W. Thomas (by invitation): Sensations of all types are normal. The biceps and triceps reflexes are hyperactive, but there is no clonus. The pupils are regular and react well to light. There is no involvement of the cranial nerves except that of the optic nerve. One of the ophthalmologists suggested that the peculiar quadrant defects might represent a lesion in the optic tract which might be due to a gumma, but the others seemed to think the condition was truly a primary atrophy of the optic nerve. There are no signs referable to the dorsal columns. The patient has been examined very carefully neurologically. The only neurologic signs present are pyramidal tract signs. The abdominal and cremasteric reflexes are present. The Wassermann reaction of the spinal fluid was 4 plus with 1 cc. and 0.5 cc. and plus-minus with 0.1 cc., and the colloidal gold curve was flat. The same type of curve is often found in patients with tabes dorsalis with involvement of the posterior column when the activity has begun to die and the reflexes are already absent.

Dr. Luis Perelman (by invitation): Clinically the condition could be multiple sclerosis. Serologic changes are found in the spinal fluid of patients with multiple sclerosis. The description of Erb's spastic paraplegia as found in the textbooks, as Dr. Thomas pointed out, is probably rare clinically. It is likely that the condition would have been considered multiple sclerosis if there had not been the serologic changes and I had not been conscious of neurosyphilis. Was the possibility of multiple sclerosis discussed at all?

Dr. Evan W. Thomas (by invitation): Three neurologists saw the patient, and the question of multiple sclerosis was always brought up, but not a single one would entertain that diagnosis because they were able to demonstrate only the pyramidal tract signs and the atrophy of the optic nerve. Every one agreed that the condition was a spastic paraplegia due to a disease of the upper motor neurons. The question arose as to whether this was due to syphilis. In view of the fact that the ophthalmologists concluded the condition was a primary atrophy of the optic nerve due to syphilis and that there was a definite positive Wassermann reaction, the disease was considered to be syphilis. There may be other changes in the spinal fluid in multiple sclerosis, but there is not a positive Wassermann reaction.

Dr. Isadore Rosen: The case is interesting because of the pupillary observations. According to the history, the pupils were normal, and it is unusual to find primary atrophy of the optic nerve, in my experience, without pupillary disturbances.

DR. EVAN W. THOMAS (by invitation): The man is not totally blind. I believe that the visual acuity was 20/200 on the left and 20/100 on the right. In my experience it takes almost complete blindness to cause absence of the pupillary reflexes.

DR. LUIS PERELMAN (by invitation): I want to contribute some information which would bear out what Dr. Thomas has said. In a number of patients examined by the board of health who had various degrees of primary atrophy of the optic nerve, functionally intact pupils have been found. Even in patients with only light and shadow vision left, there was a normally reacting pupil.

DR. EVAN W. THOMAS (by invitation): I cannot agree that dementia paralytica and tabes are meningovascular in the same sense. Dementia paralytica is a meningoencephalitis. The vessels are always involved, but there is always a decided atrophy of the parenchyma, and hordes of spirochetes are observed in the parenchyma of the brain. No one has ever found spirochetes in the dorsal columns of the cord. That indicates a difference. Here is another interesting point. If a man with clinically severe dementia paralytica is given malaria, he may recover. Such cases have been described. In an instance which I recall, a man functioned well and remained well for twenty years. At autopsy the brain showed atrophy from the former injury of the brain and he could not have functioned with that brain without treatment. There is no treatment like that for advanced tabes dorsalis, as far as I know.

Postarsphenamine Jaundice. Presented by DR. NATHAN SOBEL.

W. K., a man aged 36, is presented from the Lower West Side Social Hygiene Clinic of the Department of Health. The patient was previously presented before the Section of Dermatology and Syphilis in a symposium on syphilis on Feb. 24, 1939 (ARCH. DERMAT. & SYPH. **40**:611 [Oct.] 1939). Since that time the Wassermann reaction has been 3 plus, while at the previous presentation it was 1 plus. After seven injections of arsphenamine (average dose, 0.3 Gm.) symptoms of nausea and epigastric pressure developed. Seven days after the last injection the patient showed marked icterus. The urine gave a strongly positive reaction for bile. The edge of the liver was palpable about 2 fingerbreadths below the costal margin but not tender. Since then the patient has received three injections of sodium thiosulfate, 1 Gm. per dose, and one injection of a bismuth preparation.

DISCUSSION

DR. LEO SPIEGEL: This case of jaundice resulting from the administration of an arsenical is the first one of its kind that I have encountered in years. I asked the patient whether he had been directed as to his dietary regimen before or after the arsenical was given. He said that he was told not to eat anything for three hours prior to the injection and also after the injection. Such directions are not in my method of procedure. Some observers (Luke) have stated that a high carbohydrate diet increases the tolerance of the arsphenamines. Craven said that a diet high in fat and protein provides maximum protection against injury to the liver from the arsenicals. I instruct my patients to have a light breakfast, and I advise them to take some carbohydrate, usually milk chocolate, one-half hour before the injection of the arsenical. I have not observed the development of jaundice in over six or seven years. Arsenic has a predilection for the liver, and when carbohydrates are given before the injection the liver is filled with glycogen and thereby jaundice, which was customarily observed after the giving of arsenicals, is prevented.

DR. FRANK E. CROSS (by invitation): In the past four years I have observed about 8 cases of jaundice, whereas before that time I do not remember having encountered a case in about six years. I think the jaundice is probably due to the kind of arsphenamine used in treatment of these patients. I believe the type of arsphenamine administered is an important factor as to whether or not jaundice will develop.

DR. E. W. ABRAMOWITZ: Jaundice may develop in a syphilitic patient before arsphenamine is received as a result of either a syphilitic hepatitis or a nonspecific duodenitis (the latter may assume almost epidemic proportions). After the administration of arsphenamine jaundice may be due to an arsenical hepatitis, a Herxheimer reaction or a coincidental disease of the biliary tract. On general principles, in case jaundice develops I stop the treatment with arsphenamine. I have tried feeding patients sugar, I have been told to give them proteins and I have been told to starve them. I think it is difficult to say what is best to do. Let the jaundice subside and then begin treatment cautiously to see whether an arsenical can be tolerated later.

DR. NATHAN SOBEL: In reference to what Dr. Spiegel said, I usually tell the patients to take some carbohydrate one hour before the injection. This patient apparently did not follow instructions. Recently in the clinic 5 or 6 patients were seen within several weeks in whom jaundice developed, whereas previously no jaundice was seen for a considerable period. According to the literature, it seems to be every one's experience that cases of jaundice are not observed for a while, and then a number of them appear. The administration of arsphenamine to this man was stopped a few weeks ago, and a few injections of sodium thiosulfate were given, but he was also given a bismuth preparation because if antisyphilitic treatment is stopped in these early conditions, acute syphilitic meningitis may develop. After several months of treatment with bismuth preparations, in previous cases, small doses of arsphenamine were tried again. In every case the patients were able to tolerate full arsphenamine treatment later. However, if jaundice should develop again after the second attempt, that is a permanent contraindication for further arsenicals. The initial Herxheimer reaction this man had was a reaction to the first injection of arsphenamine. He never showed any further reaction after that. The cause of jaundice in any individual case is not known, as Dr. Abramowitz pointed out, as there may be many causes.

Congenital Syphilis; Juvenile Dementia Paralytica; Interstitial Keratitis.
Presented by DR. LEO SPIEGEL.

L. D., a girl aged 18, presented from Bellevue Hospital, has congenital syphilis. The diagnosis of juvenile dementia paralytica was first made in January 1935. From that time to August 1936 she received twenty-one injections of tryparsamide (2 Gm.) and ten injections of a bismuth preparation. In August 1936 the patient was admitted to Manhattan State Hospital for malarial therapy and underwent nine chills. After the malarial treatment, she received thirty injections of a bismuth compound and twenty injections of neoarsphenamine (8.1 Gm.).

In November 1937, while the patient was being treated a clouding of the left cornea developed, which was diagnosed as interstitial keratitis. Treatment with neoarsphenamine and bismuth preparations was continued from that time throughout 1938. The keratitis improved slightly during this time. In August 1938 a clouding of the right cornea was noted for the first time. At this time she was receiving both bismuth subsalicylate (2 cc.) and neoarsphenamine (0.45 Gm.) each week, which treatment was continued to October 15, and then she was given mercury inunctions for six weeks. At the end of her course of mercury inunctions, she was admitted to Bellevue Hospital. From Dec. 21, 1938, to the present time she has received twelve injections of arsphenamine (0.3 Gm. each) and one injection of a bismuth preparation. The keratitis has definitely improved but is not entirely healed as yet, according to the latest report from the ophthalmic clinic.

At the Neurological Institute of New York in January 1936 the Wassermann reaction of the blood was 4 plus. Examination of the spinal fluid showed the Wassermann reaction to be 4 plus in all dilutions, the cell count 5, the globulin content 1 plus, the total protein 58 mg. per hundred cubic centimeters and the colloidal gold curve 5554332100. At Bellevue Hospital the Wassermann reaction of the blood on April 19, 1939 was 4 plus. On Feb. 1, 1939, the Wassermann reaction of the spinal fluid was 4 plus in all dilutions. There were no cells or

globulin and the colloidal gold curve was 2211000000. A roentgenogram of the heart and the aorta on Dec. 28, 1938 was normal.

DISCUSSION

DR. EVAN W. THOMAS (by invitation): The case is presented chiefly because an interstitial keratitis developed after the patient had had malarial treatment. The diagnosis of juvenile dementia paralytica was definite. The condition was greatly benefited by the malarial therapy, but even with the decided improvement in mental and emotional symptoms the interstitial keratitis developed.

DR. FRANK E. CROSS (by invitation): I think the condition in this case is malignant syphilis. A varied program of therapy must be kept up, using different drugs and different types of arsphenamine (such as silver arsphenamine and possibly in this case acetarsone), along with large doses of iodides intravenously. I should also recommend courses of mercury preparations and would treat the patients persistently without rest periods, in order to prevent complications.

DR. HERMAN GOODMAN: Are all this patient's symptoms due to syphilis? There may be a patient with syphilis who shows symptoms which are not due to Spirochaeta pallida or who has a disease not caused by S. pallida. In former times, it is true, many clinical conditions were ascribed to syphilis. Alopecia areata is still held by some foreign authors to be syphilitic. Strangely, interstitial keratitis in the older books was taught to be possibly due to something other than syphilis. May not the treatment given this patient be the cause of the clinical signs of interstitial keratitis, just as in the case presented by Dr. Thomas the osseous lesions might have been due to the treatment rather than to the syphilis? Thus when the symptoms do not disappear more treatment is given, with the result that more symptoms occur, leading ultimately to symptoms which are nonsyphilitic and which are not helped by antisyphilitic therapy, which in turn causes further symptoms.

DR. EVAN W. THOMAS (by invitation): I agree decidedly that etiologic factors other than syphilis ought to be looked for in the first case in which periostitis developed during treatment and in this case of interstitial keratitis. I have asked the orthopedists what other than syphilis could cause periostitis and got no answer, but I agree it certainly should be considered. One should not be absolutely dogmatic about saying that the condition is a syphilitic periostitis. In the present case, there is a note on the chart by the ophthalmologist to the effect that he does not believe that the condition is an interstitial keratitis. It is a deep process, similar to the interstitial keratitis of syphilis, but he advises looking for foci of infection. I have looked. Tuberculosis has been definitely ruled out. Furthermore, the patient is getting better. Maybe she would have recovered anyway. She has better vision now in the left eye. Until I can find some other cause, I am going to treat the disease that usually causes periostitis in the one case and the disease that usually causes interstitial keratitis in the other case.

BROOKLYN DERMATOLOGICAL SOCIETY

MORTIMER J. CANTOR, M.D., *President*

SEYMOUR H. SILVERS, M.D., *Secretary*

April 17 and May 15, 1939

Senile Elastosis and Acrodermatitis Chronica Atrophicans. Presented by DR. ABRAHAM WALZER.

M. C., a man aged 63, a carpenter, came to the dermatologic clinic of the Jewish Hospital about three weeks ago, complaining of an infection on the right cheek, pigmented patches on the face and neck and lesions on the lower extremities.

As presented tonight, he shows a follicular infection of the right cheek which has improved considerably. The pigmented patches are on the back of the neck, about the eyebrows, on the skin adjacent to the inner canthus of each eye and on the helix and anthelix of each external ear. The color varies from ivory white (ears, eyebrow area) to yellow (neck). The white areas are smooth, soft, sharply outlined and not elevated or only faintly elevated. The patch on the neck feels thickened but soft, and the natural cutaneous folds are accentuated. There is no suggestion of a papule as the primary lesion, though there are a few scattered pigmented points (level with the skin) surrounding the patch on the neck.

On the posterior part of the hard palate and on the soft palate is a patch composed of tiny telangiectatic points on a yellow pigmented surface.

On the lower half of the trunk and on both lower extremities, extending to the toes, is an extensive diffuse atrophic dermatitis. All stages of this dermatitis can be seen, from bright red to dusky blue erythema and from raised, inflammatory boggy patches (lumbar region) to thin, wrinkled skin. The subcutaneous veins stand out prominently. The icteric index and the valves for total and free cholesterol and for sugar were within normal limits. The urine showed no abnormalities.

A section taken from the lesion on the neck showed atrophy of the epidermis with flattening and disappearance of the papillae. Immediately beneath this was a mass of degenerated elastic tissue extending across the section in a bandlike area. The elastic fibers were thickened, broken and twisted.

DISCUSSION

DR. M. L. WEITZ, Jamaica, N. Y.: As far as the lesion on the right cheek is concerned, one must consider the possibility of basal cell epithelioma. Until a biopsy is done, however, I do not think a diagnosis can be made.

DR. JACOB SKEER: The location of the lesion along the neck and the color of the lesion fit in with the description of pseudoxanthoma elasticum. On the other hand, one of the diagnostic characteristics of that condition is that it does not occur at the sites of true xanthoma, and this man has lesions on the eyebrows, on the ears and on the soft palate. The histologic report should clarify the diagnosis. The retina should be examined for angioid streaks. I do not know exactly how to classify the yellowish infiltrated lesions on the eyebrows. They fit into the picture of any of the fatty degenerative processes.

DR. A. M. PERSKY: Clinically I think the diagnosis rests on the histologic study of tissue removed from lesions in various sites.

DR. DAVID M. DAVIDSON: Cutaneous changes like those on the patient's neck are seen in senile elastosis as well as in pseudoxanthoma elasticum. One must, however, admit that the changes on the neck, eyebrows and palate are the same and are expressions of the same condition. Pseudoxanthoma elasticum does not occur on the face; senile elastosis does. The age of the patient is in favor of the diagnosis of senile elastosis. The pathologic changes are similar in these two diseases. and a differential diagnosis based on pathologic study alone is difficult, although the elastic tissue is said to be more superficially located in senile elastosis.

DR. ABRAHAM WALZER: Senile elastosis means senile changes in the skin occurring usually after the age of 40 years. Pseudoxanthoma elasticum, on the other hand, is invariably a disease of the young adult. Senile changes in the skin occur in two main forms. One is simple thinning and wrinkling, producing transparency, so that the cutaneous vessels can be seen. In the other type, as in this case, there is thickening of the skin, which usually implies senile atrophy plus external exposure to changeable weather. This type occurs in seamen, peddlers and other persons excessively exposed to the elements. This patient is a carpenter, but most of his work is outdoors.

As to the histopathologic picture, it is true that senile elastosis and pseudoxanthoma may show similar pictures. Nevertheless, pathologic study in conjunction with the clinical picture usually makes it possible to differentiate the two

conditions. Atrophy of the epidermis and elastic changes high in the section of skin speak more for senile elastosis than for pseudoxanthoma elasticum.

Against pseudoxanthoma elasticum, therefore, are the following points: the age of the patient, the lesions on the face, the color of the facial patches, the absence of primary papules, the histologic picture of epidermal atrophy and the characteristic layer of degenerated elastic tissue high in the section, directly beneath the basal layer.

The lesion on the cheek is a simple infection which is rapidly subsiding.

There is nothing I can say about the acrodermatitis atrophicans except that it is rather extensive. Its association with senile keratoses is interesting because of a common elastic tissue disturbance.

Schamberg's Disease (Unilateral). Presented by DR. L. FRUCHTBAUM.

P. F., a girl aged 9 years, was seen at the Lutheran Hospital in January 1939, complaining of an eruption on the left forearm, of nine months' duration. The flexor surface of the left forearm was covered with patchy lesions of varying sizes. There were reddish and purplish elements within the patches, giving the appearance of purpura. Of late the lesions have become paler and the redness has disappeared, and at present the lesions have diminished and have assumed a brownish tint. A blood count showed 3,760,000 red cells per cubic millimeter, with 67 per cent hemoglobin, and 3,550 white cells per cubic millimeter, with a differential count of polymorphonuclears 45 per cent, lymphocytes 48 per cent, eosinophils 2 per cent and macrocytes 5 per cent. The bleeding time was one minute and fifty seconds. The coagulation time was five minutes and ten seconds. The platelet count was 206,800. The Wassermann and Kahn reactions were negative. A roentgenogram of the cervical part of the spine taken to ascertain whether cervical rib was present failed to reveal that anomaly.

DISCUSSION

DR. ABRAHAM WALZER: I cannot see why this case is presented as an instance of Schamberg's disease. There is no resemblance to that condition. My impression is that the eruption is either linear lichen planus that is fading or a linear nevus. I think that histologic examination of a piece of tissue would help considerably in the diagnosis.

DR. MORRIS M. ESTRIN: If the eruptions were located on both lower extremities with a history of progression with redness and with final fading into yellowish brown lesions, I should consider Schamberg's disease, but the fact that the eruption is on the upper extremity makes me disagree with that diagnosis, in spite of the fact that the condition followed involvement of the lower extremities. It may be fading lichen planus or a nevus; or possibly it is some hemorrhagic disturbance, trauma or old herpes zoster. I should not consider a diagnosis of Schamberg's disease.

DR. JACOB SKEER: I think that probably a pigmentary analysis of the lesions would be enlightening. In other words, a Perl test should be done to find out whether iron pigmentation is present. If the results were positive, it would probably indicate some pigmentary disturbance. If the dopa reaction were positive, the melanin would cause one to consider pigmented nevus. I have never seen Schamberg's disease of this type. Schamberg's disease is known to be a disturbance which does not fade but progresses to atrophy, with purpuric puncta, telangiectasia and pigmentation. Even Majocchi's disease cannot be considered in this case. In my opinion, the condition is either a chronic lichenoid pigmentary disturbance or the remains of an inflammatory process.

DR. DAVID M. DAVIDSON: There is an active lesion on the dorsum of the little finger which is slightly elevated and purplish. Were the lesions on the forearm the same originally? Early lesions of Schamberg's disease do not have this appearance.

DR. SEYMOUR H. SILVERS: I should like to mention a case which has been under my observation for the past two months, that of a young woman who presents lesions identical with those of this patient. Along the ulnar surface of the left upper extremity there are patches of various shades and colors. The eruption started as typical linear lichen planus nine months ago, and the pigmentation has remained.

DR. L. FRUCHTBAUM: Three or four diagnoses have been offered for consideration. A postinflammatory process has been suggested. During the past three months there has been no evidence of inflammation. The patient has never complained of itching, pain or other disturbance. As for lichen planus, there have at no time been any papules resembling it, and there is no evidence that the process has been going down to depigmentation as a residue. There are now new lesions. This has been going on for the past three months. Some of the old lesions have faded, and a new crop has appeared. The lesions merge to form a patch and create various colors—deep blue, purple and red. If the condition were nevus, the process would be stationary. As to urticaria pigmentosa, there is no inflammation or itching, and the general appearance of the lesions is not that of urticaria pigmentosa. Several months ago I presented a patient with similar lesions, but on the lower extremities. My impression of this case is that it is an unusual one of Schamberg's disease.

Tabes (Charcot Knee; Atrophy of the Optic Nerve; Chorioretinitis). Presented by DR. ABRAHAM WALZER.

C. F., a woman aged 49, married but never pregnant, came to the clinic of the Jewish Hospital because of inability to bear weight on her left knee. There was no history of any previous illness or of any primary or secondary manifestations of syphilis. In 1935, one year before her appearance at the clinic, she had been in an accident, after which her left knee became painful and swollen. The Wassermann reaction in 1936 was negative.

Examination at present reveals pupils that do not react to light but do react in accommodation. The left fundus shows atrophy of the optic nerve, and the right, diffuse chorioretinitis. The knee and ankle jerks are absent. The Romberg test gave a positive result. The finger to nose test shows ataxia. The gait is ataxic and spastic. The sense of position of the toes is impaired. The vibratory sense is impaired. The heart and lungs are normal.

In 1936 the Wassermann reaction of the blood was negative, but that of the spinal fluid was 2 plus. Examination of the spinal fluid disclosed no cells, a negative reaction for globulin, a value for total protein of 23 mg. per hundred centimeters and a colloidal gold curve of 22222000000. In 1937 another examination showed the Wassermann reaction to be 4 plus; the reaction for globulin was negative; there were no cells, and the colloidal gold curve was 4422211110.

A roentgenogram of the left knee showed advanced hypertrophic changes with increased density of the articulating and adjacent portions of the joint. The joint body presents calcification and ossification of the medial lemniscus (Charcot joint with osteoarthritis).

The results of treatment were unsatisfactory, because of the patient's irregular attendance at the clinic.

DISCUSSION

(The diagnosis was accepted.)

Recurrent Cellulitis Resulting in Chronic Lymphedema. Presented by DR. A. M. PERSKY.

R. S., a Negro aged 29, was admitted to the King's County Hospital on March 27, 1939, complaining of pain, malaise, anorexia, fever and swelling of the right leg of several days' duration. He had had a number of similar attacks, involving both legs, from the age of 8 years until four years ago, when he came

to New York from North Carolina. The attacks usually appeared in the spring, and recovery was apparently complete in several days. He had had no attacks since coming to New York, but three years ago he had an "operation" for an enlarged inguinal gland.

Examination showed an acutely ill patient with a temperature of 102 F. The condition of the right leg appeared like acute cellulitis with deep thrombophlebitis. With rest in bed, local wet dressings and administration of sulfanilamide by mouth, recovery ensued in ten days. Roentgenograms of the legs were normal. The patient now shows decidedly stretched skin on the legs, hanging in folds over the infiltrated subcutaneous tissue. There are no enlarged inguinal glands.

DISCUSSION

DR. SEYMOUR H. SILVERS: The skin on one of the legs is relaxed, but I am sure that this is not a case of cutis laxa, or Ehlers-Danlos syndrome, for none of the classic signs of this syndrome are present. This man had elephantiasis of both legs, of unknown cause. Three years ago I studied two brothers and their father who had conditions similar to that shown by this patient. They had Milroy's disease, which is familial. I questioned the patient in the present case, and he gave no familial history of this condition or anything similar to it. Nevertheless, I am inclined to think that this case fits into the picture of Milroy's disease. The other two boys had attacks similar to those which this patient described. There were sudden attacks of swelling which looked like erysipelas or cellulitis, accompanied by high temperature and extreme pain. These attacks would occur as often as once in three months. Various studies were made, but no etiologic factor could be determined.

DR. L. FRUCHTBAUM: During the past few years I have observed several such cases of lymphedema, and in all of them the condition started like erysipelas. The patient in this case is a Negro, and therefore one could not see the characteristics of erysipelas. Examination of the toes of this patient reveals a classic picture of dermatophytosis. This I have noticed also in my own cases. I think more attention should be paid to infections between the toes in order to check a recurrence of the attacks.

Unilateral Acrocyanosis. Presented by DR. L. FRUCHTBAUM.

S. G., a woman aged 34, was seen at the Lutheran Hospital on March 16, 1939, complaining of swelling and discoloration of the left hand and fingers for the past year. There are definite swelling and dark bluish discoloration of the left hand and fingers, particularly on the dorsum of the hand. There is increased sensitivity to touch of the left hand. There is no pain or itching. The left hand feels cold. There is no blanching on raising of the left arm.

On examination the blood pressure and the pulse were equal on the two sides; the blood pressure was 175 systolic and 100 diastolic. The Wassermann reaction of the blood was negative. The urine was normal. The basal metabolic rate was +7 per cent. A roentgenogram of the cervical portion of the spine did not reveal cervical rib. A roentgenogram of the left hand showed hypertrophy of the joints.

DISCUSSION

DR. DAVID M. DAVIDSON: Besides the cyanosis there are definite atrophy and wrinkling of the skin, and I consider this case one of acrodermatitis chronica atrophicans. It presents two rare and interesting features, the unilateral distribution and the osseous changes.

DR. C. THOMAS CHIARAMONTE: I wish to mention the fact that between the third and the fourth finger there is pronounced erosio blastomycetica.

DR. L. FRUCHTBAUM: I presented this case to rule out the presence of cervical rib in a unilateral cutaneous lesion. One seldom sees acrocyanosis on one side of the body only. The patient complains of nothing but loss of sensation

in the hand. The roentgenogram of the hand shows no arthritis but reveals hypertrophy and a large number of blood vessels. Obviously there is some obstruction to circulation of the blood in the hand which causes the present condition.

1. Late Secondary Syphiloderm. 2. Syphilitic Osteitis? Presented by DR. M. DICKMAN.

A. W., a Negro aged 48, is presented from the Jewish Hospital. The patient states that he had a chancre about twenty years ago. In 1927 he complained of abdominal pains and because of a positive Wassermann reaction received six injections of neoarsphenamine and six of a bismuth compound, with improvement in his symptoms. In 1930 he went to the Department of Health Clinic because of abdominal pains and received treatment for two years. During this time his symptoms were relieved. In 1933 they returned. In 1934 he received six months' treatment by a private physician. From May 1938 to February 1939 he received twenty injections of a bismuth compound and twenty of neoarsphenamine at the Jewish Hospital.

He presents a single annular lesion the size of a silver dollar in the episternal notch. The border of the lesion is composed of edematous erythematous papules, the center being hyperpigmented.

This lesion developed in February 1939 and has increased to its present size in spite of five injections of a mercury compound and five of a bismuth compound. In June 1938 there were three similar annular lesions, two on the left side of the chest and one on the right arm. These lesions disappeared in about two weeks under arsenical therapy. Histologic examination at that time showed dense collars of plasma cells about the blood vessels, and a pathologic diagnosis of a secondary syphiloderm was made.

A roentgenogram of the pelvis taken in April 1938 showed decided increase of osseous density of the entire left half of the pelvic girdle, the most pronounced condensation appearing in the region of the lower part of the ilium and the ischial bones. In the ischial and pubic bones there were small irregular areas of lessened density.

DISCUSSION

DR. DAVID M. DAVIDSON: A few months ago this patient presented a lesion on his chest similar in outline and consistency to the lesion now present on his neck. At that time I was doubtful about the syphilitic origin of the lesion, because of its edematous appearance and consistency; pathologic study of the lesion, however, proved it to be a secondary syphiloderm, and it promptly disappeared under arsphenamine therapy. The present lesion appeared while the patient was receiving injections of a bismuth compound and does not regress, although this treatment is continued. This patient is probably bismuth resistant, and the lesion will disappear as soon as he again receives arsphenamine therapy.

DR. M. DICKMAN: The lesion on the neck must be accepted as a late secondary syphiloderm because of the characteristic pathologic picture. The involvement of the left innominate bone was considered as a possible manifestation of Paget's disease or as a metastatic process from a malignant process of the thyroid or of the prostate. As these conditions were excluded by careful study, one must, by exclusion, consider this process a syphilitic osteitis.

A Case for Diagnosis (Bowen's Disease? Superficial Epithelioma?). Presented by DR. M. DICKMAN.

R. T., a woman aged 75, is presented from the Jewish Hospital. She shows a single arciform flat erythematous patch the size of a silver dollar on the left side of the sacral region of the back. There are many hard, yellowish crusts on the surface, especially at the edges. Slight atrophy is present in the center of the lesion.

This lesion appeared about six years ago and has increased slowly in size. The patient complains of moderate itching of the patch. Topical applications are the only treatment she has received in the past two years.

DISCUSSION

DR. ABRAHAM WALZER: It is difficult to make a diagnosis of Bowen's disease clinically; for that reason either an epithelioma or Bowen's disease was suggested. I should like to know about the therapy in this particular case.

DR. L. FRUCHTBAUM: I do not think the condition requires any therapy.

DR. A. M. PERSKY: I should either use wide electrodesiccation (about ½ inch [1.3 cm.] beyond the margin) or excise the lesion.

DR. JACOB SKEER: I have found that such lesions respond poorly to roentgen and radium therapy. Probably desiccation is the method of choice.

DR. M. L. WEITZ, Jamaica, N. Y.: I feel as Dr. Fruchtbaum does regarding therapy in a case like this. I think the lesion should be left alone. The patient is old, and the lesion has been present for five or six years. It is not causing any discomfort or pain.

DR. MORTIMER J. CANTOR: This is a case of Bowen's disease, which should never be left alone. The lesion should be desiccated and curetted completely.

DR. M. DICKMAN: Material for a biopsy was taken, and the histopathologic report was epithelioma in Bowen's disease. In this case I believe that excision of the entire lesion is the treatment of choice.

Multiple Superficial Epitheliomatosis. Presented by DR. H. L. FEIGENBAUM.

M. H., a widow aged 65, born in the United States, states that her present lesions started fifteen years ago, at which time several small reddish areas appeared on the forehead and cheeks. These developed slowly, and nine years ago a small (cystic?) lesion developed on the right cheek. This was removed with radium. Similar but flatter lesions developed on the forehead and other parts of the face. These were treated with twenty to thirty applications of the roentgen rays. Itching was present at times. The past history was irrelevant.

The patient presents multiple yellowish red macular and flat papular lesions on the forehead and cheeks varying in size from that of a split pea to that of a lentil and slightly larger. Some have coalesced by peripheral extension to form irregular, larger patches. Scaling is present in practically all. In the center of the forehead there is a large patch showing crusting, which has been traumatized by scratching. The right cheek presents a white scar at the site of the removed cyst (?) nine years ago. In addition, there are several patches of senile keratosis. The dorsa of the hands present several superficial erythematous lesions similar to those on the face.

Lupus Vulgaris. Presented by DR. JACOB SKEER.

J. M., a man aged 61, born in Poland, came to the Israel-Zion Hospital complaining of an eruption on the face of twenty years' duration.

The patient has had hay fever for five years and had pneumonia in 1937.

Examination shows an irregular circular lesion the size of a half-dollar in the left temporal region, crossing the outer half of the eyebrow and the upper lid and completing the circle on the temple. The margin is made up of firm, red-brown nodules the size of millet seeds and about three or four deep. Some of the nodules are crusted, and diascopic pressure shows the apple jelly color. The center is slightly edematous and covered with fine scales, but no nodules can be seen. An oval similar patch is present on the left side of the lower jaw, near the chin.

A roentgenogram showed clouding of the apexes of both lungs but no active process.

The histologic diagnosis was lupus vulgaris.

DISCUSSION

DR. C. THOMAS CHIARAMONTE: I agree with the diagnosis as presented. I feel that a diet free of salt is of value in such a case.

DR. L. FRUCHTBAUM: I cannot suggest any therapy that has been successful in my own experiences.

DR. ABRAHAM WALZER: This is a type of lupus vulgaris, but I think it belongs to the Leloir type of lupus erythematosus. From the first glance at this patient lupus vulgaris would never enter any one's mind. There is a definite appearance of atrophy, and the lesion looks erythematous.

DR. MORTIMER J. CANTOR: I think a condition like this would do well with ultraviolet irradiation with a water-cooled quartz mercury vapor arc lamp, the exposure starting with thirty seconds and increasing to sixty or eighty seconds once a week, with pressure for ten or twelve treatments. I have seen improvement from this treatment in a number of cases. The treatment should be given to the cheek and forehead and not to the eyelid.

A Case for Diagnosis (Eruption Resembling Granuloma Annulare). Presented by DR. JACOB SKEER.

D. T., a boy aged 7, born in the United States, was brought to the Cumberland Hospital complaining of an eruption of two years' duration.

The patient had measles, pertussis, chickenpox and "running ears" as an infant. He had a "heat rash" when he was 2 years old. The mother stated that he had head colds frequently.

The mother has lichen planus.

The eruption seen in the boy is varied and polymorphous and is described as grouped, discrete pinhead-sized papules on the anterior and lateral aspects of the neck. Several erythematous lesions with ringed papular margins are distributed on the arms, forearms, thighs and legs. A large patch (5 by 6 cm.), mildly erythematous and made up of pinhead-sized conical papules and atrophic spots, is situated on the chest, below the ensiform cartilage and the margin of the ribs. A similar patch is situated over the dorsal portion of the spine, and there are several smaller lesions on the back and the abdomen.

The condition began on the outer aspect of the left ankle, which now presents an irregular rectangular area, sharply defined and slightly hyperkeratotic.

The reaction to tuberculin was negative with dilutions of 1 : 1,000,000, 1 : 100,000 and 1 : 10,000.

A roentgenogram of the chest showed the shadows of both hili to be accentuated, with several small calcific deposits and accentuation of the inferior root, trunk and branches.

DISCUSSION

DR. DAVID M. DAVIDSON: If I had not seen the lesions on the body but had looked at only those on the extremities, I should not hesitate to make a diagnosis of granuloma annulare. I cannot make up my mind as to the lesions on the trunk. The patches show distinct papules at their peripheries, but the papules are much smaller than those usually seen in granuloma annulare. I am unable, however, to suggest any other diagnosis.

DR. L. FRUCHTBAUM: I do not think one is justified in making a diagnosis of this lesion without a biopsy. The early lesions are nodules. The eruption probably is a form of cutaneous tuberculosis.

DR. ABRAHAM WALZER: All the lesions on the body are of one type. They are scattered over the trunk and extremities and are tiny papular lesions that disappear under pressure. They have a tendency to grouping; eventually they form a small ring or groups, as on the forearm, and then progress further, producing larger rings and patches. I think the whole process is one. I confess I cannot exactly classify this condition with any entity that I know of, but I wonder

whether it does not fit into the group of dermatoses described under the head of annular erythemas of Lipshütz or Darier. However, I think this condition is an acute inflammatory process and not granuloma annulare.

DR. DAVID M. DAVIDSON: Perhaps I did not make myself clear. I did not mean that the patient presents two conditions. I stated that I have not seen granuloma annulare produce such lesions as those on the trunk of this patient, but I consider them part of the same process as those on the extremities.

DR. C. THOMAS CHIARAMONTE: I observed a case about one month ago in which the patient had a lesion similar to the one on this patient's left ankle. It was a wide plaque with a typical raised granulomatous border that was smooth all around, and the center was dotted with pinhead nodules which had become pigmented. The biopsy specimen was reported as representing granuloma annulare. This may be an unusual type of that disease.

A Case for Diagnosis (Moniliasis?). Presented by DR. MORTIMER J. CANTOR.

M. S., a married white woman aged 31, was first seen on May 11, 1939, at the Beth Moses Hospital Dispensary. The past history was of no importance.

The first eruption dates back three years, when the patient noticed three small spots, one on the right cheek, one on the left breast and one on the flexor surface of the forearm. Within three months the eruption became widespread, covering the upper and lower extremities and the torso in irregular patches of papulovesicular oozing dermatitis. She was treated with various salves and lotions irregularly at other institutions for a year and a half, with little improvement. She then went to a private physician, who "cleared up the condition with diet, internal medicines and salves," leaving pigmented spots. The patient remained free from lesions for about six months.

The present eruption began about September 1938, with moist, elevated, infiltrated patches on both areolas, and spread to its present extent. Little treatment was given until April 1939, when four roentgen treatments were administered to both breasts, one each week, the last one having been given about May 1, with practically no effect on the eruption.

The patient is normally developed. The upper and lower extremities have variously sized circinate and spotty patches of variegated brown discolorations covered with fine furfuraceous scaling; these are the remains of the original eruption. There are no signs of pruritus.

On both breasts, mainly about the areolas but also involving the glabrous skin, are many papulovesicles ranging in size from that of a large pinhead to that of a lentil, some being considerably more elevated than others. Many of the flatter ones are red and exceedingly moist. The latter type makes up the majority of the individual lesions. The patches, which are mostly confined to the areolas and especially to the left side, vary from the size of a pea to about that of a silver quarter and are composed of the flat-topped, drier papules. The color of these papules varies from brownish red to yellowish brown, and many, especially the moist ones, are covered with a yellow-brown, sanguineous impetiginous crusting. The patches are considerably elevated, fungoid and papillomatous.

The patient's tongue is moist and is irregularly furrowed throughout its extent with areas of hyperkeratosis and depressions which give the appearance of being denuded of epithelium.

The laboratory reports were as follows: The Wassermann reaction was negative. The urine was normal. Cultures of material taken from the tongue and from the lesions have not yet been reported on. The result of the oidiomycin test was positive. A direct smear of material from the tongue showed a network of branching and filamentous hyphae and yeastlike organisms (Oidium albicans). A direct smear of material from the lesions on the breast was negative for Monilia or hyphae. A biopsy specimen taken on May 11 showed nothing characteristic. A tuberculin test done on May 27 with a dilution of 1:10,000 gave a negative result.

DISCUSSION

DR. L. FRUCHTBAUM: I think the patient has had too much medication. She is of a neurotic type. I suggest the use of mild topical applications.

DR. SAMUEL HECHT: All I could make out was a dermatitis, and ordinarily I should have no doubt of its parasitic nature. Formerly it was called just eczema.

DR. ABRAHAM WALZER: I saw this patient a couple of years ago. At that time she had a fairly generalized eruption involving not only the areas now affected but the upper extremities and even the thighs and the lower part of the abdomen. The condition was diagnosed as some type of parasitic infection, and she was treated accordingly. The condition cleared up almost completely but broke out again. Finally the patient disappeared. She came to the Beth Moses Clinic a few days ago with the present eruption. As to the question of moniliasis, I think it is not going to be an easy matter to prove whether this is true moniliasis of the skin. If the same monilia could be obtained from the intestinal tract, from the mouth and from the lesions it would be strong evidence in favor of such a diagnosis.

Keratosis Pilaris. Presented by DR. MORRIS M. ESTRIN.

M. M., a white man aged 69, was referred to the dermatologic department of the Kings County Hospital on account of a peculiar eruption on the skin, resembling pediculosis pubis.

The past history was irrelevant except for a long history of urticaria and pruritis.

About two years ago the patient noticed pigmented papular lesions on the hairy portion of the body. They never caused him any concern except for occasional itching.

Examination reveals that on the arms, legs, chest, back, hips and upper parts of the thighs there are soft horny papules, situated around the pilosebaceous orifices. On removal of these horny plugs, a coiled hair can be seen, embedded in the sebaceous deposit in the follicle.

DISCUSSION

DR. SEYMOUR H. SILVERS: I wonder whether a biopsy of material from a hair follicle would provide a clue to the reason for the peculiar coiling of the hair. There must be some cause for the peculiar shape assumed by the hair.

DR. L. FRUCHTBAUM: I recently gave viosterol to a patient with keratosis pilaris and obtained remarkable response; so perhaps this condition is due to avitaminosis.

DR. MORRIS M. ESTRIN: I asked the man about his diet. He is peculiar in this respect. He does not like fish, milk, eggs or meat. Nothing smells right to him. He has trouble with his nose. He has had complaints for the last two or three years. Perhaps with a new diet and vitamin A it will be possible to improve his general condition and his skin.

A Case for Diagnosis (Dermatitis Venenata?). Presented by DR. SEYMOUR H. SILVERS.

J. K., a married man aged 34, a physical therapeutist, complained of an eruption of the face and forehead of two years' duration. The eruption has changed in intensity during this period, and one year ago, while the patient was visiting in Syracuse, N. Y., the eruption cleared entirely. The patient had received various topical treatments, injections of a gold compound, roentgen therapy and various medications administered orally. Improvement has been noticed lately with roentgen therapy, a mild cream for the face and intravenous administration of calcium gluconate. The following diagnoses have been considered: lupus erythematosus, rosacea, seborrheic eczema, psoriasis and contact dermatitis. In the past

ten days a follicular papular and vesicular eruption has appeared on the upper extremities and it has now spread to the upper part of the trunk. The eruption has not been especially itchy.

The urine was normal, and the Wassermann reaction of the blood, negative. Roentgen examination of the sinuses showed them to be normal. Attempts were made to eliminate known irritants in the home.

Examination now shows swelling of the face and eyelids. The skin of the face and forehead is covered with a patchy eruption of vesiculopapular and somewhat crusted lesions. There are some patches, ranging in size from that of a dime to that of a quarter, on the sides of the face. There are some scaling and redness back of the ears. Mainly on the flexor surface of the upper extremities and on the trunk there are numerous scattered and well defined patches of pinhead-sized to dime-sized crusted and scaly follicular papular lesions. The scalp is clear, and there is an abundant growth of hair. On the sternum there is a well defined quarter-sized reddish yellow scaly lesion.

DISCUSSION

DR. MORRIS M. ESTRIN: The patient stated that the onset was due to sunburn originally contracted a few years ago. He is a physical therapeutist, with the use of plenty of apparatus. How much treatment he has given himself I do not know. I think this condition belongs to the lupus erythematosus group.

DR. L. FRUCHTBAUM: I shall venture the diagnosis of some type of tuberculosis, perhaps Lewandowsky's rosacea-like tuberculid.

DR. SAMUEL HECHT: From the appearance of the lesions I agree with the presenter's suggested diagnosis of dermatitis venenata, and I have no doubt that the patient has been using something besides what the physician prescribed for him. When the dermatitis venenata clears up, perhaps it will be possible to tell what the underlying condition was.

The fact that the patient is a physical therapeutist and is perhaps using some treatment without mentioning it must be considered.

DR. JACOB SKEER: I should like to venture a diagnosis of the Senear-Usher type of lupus erythematosus. The lesions on the back appear pemphigoid.

Von Recklinghausen's Disease. Presented by DR. JACOB SKEER.

M. R., a married woman aged 52, born in Poland, came to the dermatologic clinic of the Jewish Hospital, complaining of numerous tumors on the body.

The past history was irrelevant.

Examination shows numerous tumor-like lesions varying in size from that of a small pea to that of a hazelnut, distributed on the face, trunk and upper and lower limbs. The lesions are soft and sessile, becoming easily invaginated on pressure. Some of the lesions are the color of normal skin; others have a bluish tinge. There are several vascular nevi, as well as generalized freckling and larger and variously shaped café-au-lait patches.

DISCUSSION

(The diagnosis was accepted.)

A Case for Diagnosis (Lichen Planus Sclerosus et Atrophicus [Hallopeau])? Presented by DR. MORRIS M. ESTRIN.

M. R., a white man aged 50, is presented from the Kings County Hospital. He stated that a small papule developed on the dorsum of the left foot twenty-one years ago, while he was in the trenches during the war. The lesion grew slowly, showing activity at the border and turning white and atrophic in the center, until it reached its present size. Other lesions developed subsequently on the right foot and left hand.

The patient presents a sharply outlined palm-sized plaque on the dorsum of the left foot, with an atrophic center and a papular border. There is a coin-sized area at one corner of the lesion which is elevated and sclerotic. There are similar coin-sized lesions on the dorsum of the right foot and the dorsum of the left hand. There is a hard papule at the tip of the coccyx, with no atrophy.

Treatment for the past two weeks has been with boric acid ointment U. S. P. This has resulted in softening of the lesion.

DISCUSSION

DR. ABRAHAM WALZER: Every time a case of this kind is presented the question of scleroderma, white spot disease and lichen planus atrophicus is brought up. To permit a diagnosis of lichen planus atrophicus, a papule of lichen planus must be seen. All such conditions can be put into three groups: those that begin as a lichen papule and end in atrophy, those that begin as white spots and end in atrophy, and those that are a cross between these two, that is, those that begin as lichenoid papules and end in atrophy. In this particular case all one sees are patches of atrophy with hyperpigmented borders. There is not the slightest evidence of lichen or a lichenoid papule. The condition belongs to the white spot or scleroderma group rather than to the lichen group.

DR. SEYMOUR H. SILVERS: I do not think this is Csillag's disease. I saw this patient previously, and I suggested the diagnosis of lichen sclerosus et atrophicans. There was a great deal of discussion whether lichen sclerosus et atrophicans is a disease sui generis or whether it is related to the lichen group or to the morphea group. I think that any one may maintain either point of view and will find a sufficient number of articles to back him up. Miescher published an article (Miescher, G.: Weissfleckenkrankheit [Lichen sclerosus—white spot disease—karten blattähnliche Sklerodermia], Arch. f. Dermat. u. Syph. **171**:419-429, 1935) suggesting that this particular type of lesion belongs neither in the lichen group nor in the morphea group. It is a special disease that he called lichen sclerosus et atrophicans. However, this is not universally accepted. Miescher pointed out that in that type scattered lesions are found and some of them fit very well into the morphea-like group. Even the pathologic picture varies a great deal; some believe it fits into the lichen group and some believe it fits into the morphea group.

PHILADELPHIA DERMATOLOGICAL SOCIETY

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May 19, 1939

Virus Infection Resembling Herpes Simplex. Presented by DR. CARMEN CHRISTINE THOMAS, Wilmington, Del. (by invitation).

L. R., a Negress aged 26, well nourished and well developed, presents hypertrichosis of the face and chin. She has had recurrent attacks of grouped vesicles in crops every two or three weeks for the past ten years. These lesions result in scar formation after ten or fifteen days. There are scars of former lesions on the back, abdomen, buttocks and thighs and active herpetiform lesions at some of these sites. The patient has latent syphilis of unknown duration, for which she has received since Sept. 2, 1936, five injections of trisodium arsphenamine sulfonate and twenty-six of a bismuth compound. She had exfoliative dermatitis lasting five months in 1936 and acute pelvic inflammatory disease in 1938. Material from

a five day old herpetic lesion on the left knee was inoculated into the left cornea of a rabbit by scarification with a lancet. The right eye was scarified with a sterile lancet in the same fashion. Six days after inoculation the left eye began to exude creamy pus, and ten days after inoculation a pannus covered the entire left cornea. The right cornea remained normal. At this time (on the eleventh day) the animal became restless, the head was held flexed to the left and the right front leg became paralyzed (typical symptoms of herpetic keratitis and encephalitis).

DISCUSSION

DR. ROBERT L. GILMAN: Why may not this condition be herpes simplex?

DR. ELMER R. GROSS, Wilmington, Del.: I do not think that the lesions prove or disprove anything, because after injection one sometimes finds a traumatic reaction of the eye with leukoma as the result. I encountered this in experiments on interstitial keratitis.

DR. ERICH URBACH (by invitation): I should like to commend Dr. Thomas because she was careful to perform a control test on the other eye. One eye was only scarified, and the other was scarified and inoculated. Only the eye which was inoculated is infected and shows keratitis. Encephalitis and paralysis cannot occur without infection. Dr. Thomas has in mind the possibility of desensitization. Hruszek suggested the possibility of immunizing persons with herpes simplex. He suggested the method of Pasteur, that is, to dry the brain and the spinal cord of an infected rabbit and to inject the prepared material in increasing quantities into the skin. I have tried the same procedure in cases of pemphigus. I have dried the brain and spinal cord from an animal infected with rabies and have injected this. The difficulty is that one always tries immunization too late. Animals seem to be easily immunized, but human beings are immunized only with great difficulty. I feel, however, that the immunization experiment should be performed in this particular case.

Imbibitio Lipoidica Collageni Degenerati Cutis. Presented by DR. ERICH URBACH (by invitation) and DR. W. R. HILL (by invitation).

V. W., a white woman aged 52, presents at the external lateral surfaces of the arms, thighs and legs about a dozen indurated lesions of diversified appearance. The youngest lesion (three years old, on the external aspect of the left tibia) is about 4 mm. in diameter, elevated, hard and reddish brown. The other lesions, varying in duration from ten to thirty years, are of three types. All are definitely located in the deeper parts of the cutis; the skin over them is depressed and violet-brown; they have a cartilaginous feel. Other lesions, also situated deep in the cutis, have an elevated, keloid-like surface. Two lesions (above the right anterior iliac spine and on the left thigh) differ from all the others in that they are yellowish brown but on pressure become distinctly yellow. Clinically, these lesions resemble necrobiosis lipoidica diabeticorum. The patient had rheumatism at the age of 13; since then she has had five attacks about five years apart. The attacks have been limited as a rule to one joint, which has become red and swollen and required rest in bed for one month for relief. A tonsillectomy was done nineteen years ago. The first lesion (on the left hip) appeared thirty years ago, apparently associated with the rheumatic attack. The other lesions appeared on the arms, legs and thighs at various intervals, usually about five years apart, the last three years ago. None of the later lesions seems to have been related to the rheumatic infection. There is no history of preceding trauma. The value for total blood cholesterol was 363 mg., that for cholesterol esters 227 mg. and that for free serum cholesterol 135 mg. per hundred cubic centimeters. The sugar tolerance test gave a normal result. The blood serologic reaction of the blood for syphilis was negative. Histologic examination showed hyperkeratosis; there was abundant formation of connective tissue cells with deeply stained nuclei. The fibrils between them were condensed but contained spaces suggesting lipoid sub-

stances, which were extracted with alcohol. Other parts showed fewer new connective tissue cells, but the fibrillar tissue appeared altered (basophilic degeneration of the collagen). The small vessels had thickened walls, and the cells of the intima were swollen. The Weigert stain revealed almost complete absence of elastic tissue. The sudan IV stain showed abundant brown-red globules and granules between the fibrils of the connective tissue and rarely in the cytoplasm. There were no foam cells. The fat was soluble in ether, partly soluble in alcohol and acetone and insoluble in chloroform. Doubly refractive bodies, fatty acids, soaps and amyloid were not demonstrable by suitable methods.

DISCUSSION

DR. ERICH URBACH (by invitation): Two kinds of lipoidoses of the skin are now distinguished, the generalized and the localized. The three types of generalized lipoidoses are (1) xanthelasma, (2) extracellular cholesterinosis and (3) lipoid-proteinosis. Among the localized lipoidoses are recognized necrobiosis lipoidica diabeticorum and the cutaneous lesions which are known as "sailor's skin," which are seen in old persons exposed for a long time to the sun and wind. The histologic studies presented suggest a type of lipoidosis which I have never seen before. It shows lipoid imbibition of the degenerated connective tissue.

A Case for Diagnosis. Presented by DR. JOHN H. STOKES.

H. B., a white man aged 32, presents a slightly raised, milky white, sharply demarcated plaque of irregular outline on the glans penis, on either side of the frenum and surrounding the meatus. There is a similar lesion on the under side of the foreskin. There is no inguinal adenopathy. In 1932 the patient noticed a minute white deep-seated papule in the glans penis, just adjacent to the meatus. This disappeared spontaneously in one year. In 1937 he noted a small, slightly elevated, somewhat shriveled white lesion on the glans penis, on both sides of the frenum; during the past year it has extended. There has never been any elevation or discharge.

DISCUSSION

DR. THOMAS BUTTERWORTH, Reading, Pa.: I think this man has balanitis xerotica obliterans, although there is no obliteration of the urinary meatus. The lesion has the same whitish, slightly depressed appearance as had that in a case I presented before this society (ARCH. DERMAT. & SYPH. **35**:1162 [June] 1937).

DR. ERICH URBACH (by invitation): I agree with Dr. Butterworth's diagnosis.

DR. JOHN H. STOKES: I have seen lichen sclerosus and lichen planus on the penis produce a picture something like this. I confess I lean toward the diagnosis of lichen sclerosus. I have not seen the other condition, so that I am not able to say whether I concur in that diagnosis. The original diagnosis made by one of my associates who saw the process a number of years ago, when it first began, was kraurosis occurring on the penis and equivalent to kraurosis vulvae in women. Ormsby stated that such a condition has been described. I should not subscribe to that diagnosis. I am more inclined to look for the individual papules of lichen planus, but the histologic section certainly shows the considerable sclerosis with areas of lymphocytic infiltration which one sees at the base of the lesions of sclerosing lichen planus.

Lymphogranulomatosis (Hodgkin's Disease): Treatment with Sulfanilamide. Presented by DR. ERICH URBACH (by invitation).

S. S., an undernourished white man aged 52, presents a widespread eruption exempting only the palms and soles. It consists of thickening of the skin, which is excoriated in places or covered with branlike brownish violet scales. The face shows distinct papules and crusted lesions. There is visible enlargement of the lymph nodes of the neck, axillas and groin; the nodes are hard and not coalescent.

The condition began in January 1938, as pruritic small erythematous patches on the arms. In rapid succession similar lesions appeared on different parts of the body, until by the end of four months the entire body was involved. There was almost unbearable pruritus. Five months after the onset, generalized adenopathy was noted. There was a loss of 12 pounds (5.4 Kg.) in weight in the first six weeks of the disease. The patient was hospitalized in June 1938 at one hospital and in September and December at another. At this time a blood count showed 20,000 leukocytes per cubic millimeter, with 29 per cent eosinophils. A roentgenogram of the chest showed no evidence of glandular involvement. In September the spleen was found to be enlarged. A blood count showed 4,800,000 erythrocytes and 20,000 leukocytes per cubic millimeter, with 90 per cent neutrophils, 8 per cent lymphocytes and 2 per cent eosinophils. The sedimentation rate of the blood was 110 mm. The value for blood sugar was 85 mg. per hundred cubic centimeters. Serologic tests of the blood gave negative results. In sections there were acanthosis and edema of the epidermis. In the stratum papillare and reticulare there was perivascular infiltration of small and large lymphocytes, epithelioid cells, plasma cells and a few eosinophilic cells. The blood and lymph vessels were enlarged. The section of lymph node showed decided hyperplasia of the reticular cells. Here and there cells suggesting Dorothy Reed giant cells were present. There has been remarkable improvement under treatment with sulfanilamide (36 Gm. in nineteen days). The acute cutaneous lesions and the pruritus have almost disappeared; there has been a diminution in the size of the lymph nodes. The following data show the influence of treatment on the blood picture and on the sedimentation rate:

	1939			
	4/28	5/5	5/8	5/15
White cells	20,000	12,300	10,400	8,100
Neutrophils	90	79	65	63
Lymphocytes	8	21	21	26
Eosinophils	2	6	14	11
Sedimentation rate	110	100	125	65

DISCUSSION

DR. DONALD M. PILLSBURY: Although there were no cultural studies indicating the presence of streptococci, I think the number of cases in which such a condition responds to sulfanilamide is remarkable. Another case of generalized exfoliative dermatitis in a woman was presented tonight, in which the only reason for giving sulfanilamide was the fact that there were streptococci in the urine. I do not know why the present patient responded. Is there possibly some nonspecific effect of the drug? I think there is danger of becoming overenthusiastic about the use of sulfanilamide in such cases. I know that I have given the drug in my office on some occasions when, as I look back, I think I should not repeat the performance. I think one ought to be cautious about indiscriminate administration of sulfanilamide.

DR. ERICH URBACH (by invitation): This man was so distressed that it was necessary to take him to the hospital. He had been previously hospitalized and had received much roentgen therapy as well as other forms of nonspecific treatment. The English school believes that Hodgkin's disease is a virus disease. I used sulfanilamide on this basis. It was interesting to see the progress in this case. I gave the first course of treatment cautiously for five days, 4 Gm. daily, divided into ten doses. The treatment was then stopped, and the itching became less. The cutaneous lesions were also improved, so I waited. After four days there was a recurrence of the itching, and new lesions and fever developed. A second course was given, lasting three days. There was improvement again. I then gave 2 Gm. in two days. I cannot say whether there will be a second relapse.

Lupus Erythematosus (Extensive Discoid). Presented by DR. WILLIAM E. KELLEY, Omaha (by invitation).

J. M., a white man aged 44, shows diffuse erythema of the face, cheeks and ears. The lesions are slightly scaly, with hyperpigmented borders. The ears are red and tender, showing some atrophy of the rim. There are a few round areas of tender, red, slightly scaly patches on the back of the neck. The backs of the wrists and the forearms show bright red, slightly scaly, elevated gyrate lesions with atrophic centers. The arms and the V of the neck, the sites of previous involvement, show extensive areas of leukoderma. The edges of the lesions on the fingers are hyperpigmented. The patient was well until July 1936, when he went to the seashore for a week and received an extensive sunburn. This healed, but three weeks later little "pimples" began to break out on his face. In a few weeks the entire face, the "V" of the neck and the arms were involved. The following winter the condition cleared up completely, leaving the areas of leukoderma now seen. In the summer of 1937 it again flared up after an exposure to the sun, not so severe as the first. It cleared up again the following winter except for a small area on the left cheek. In the summer of 1938 the patient was on a farm for three days. A week later the lesions again flared up, this time with involvement of the upper lip and the backs of the wrists. Last winter it failed to clear up completely. The redness on the face and wrists persisted. A blood count showed 4,950,000 erythrocytes and 7,700 leukocytes per cubic millimeter. The value for hemoglobin was 87 per cent. A differential count showed 81 per cent polymorphonuclears, 12 per cent lymphocytes, 5 per cent monocytes, 1 per cent eosinophils and 1 per cent basophils. The Wassermann, Eagle and Kahn reactions of the blood were negative. A roentgenogram of the chest showed the bony portion of the thorax, the heart and the aorta to be normal. There were scattered diffuse, small nodular areas of fibrosis throughout both lung fields, more marked in the upper outer third. As there was a clinical history of working ten years in a sand blast, this was undoubtedly due to silicosis. There was no evidence of tuberculosis or other secondary infection. In August 1936 the patient received fifteen injections of gold sodium thiosulfate, without improvement. At present he is receiving a bismuth compound.

DISCUSSION

DR. ROBERT L. GILMAN: Some one commented that at first glance he thought the patient might have pellagra. Just what role dietary deficiency may play in this case and whether it may suggest additional therapeutic measures cannot be stated. The patient has been seen before, in other clinics. There was also some inquiry about the status of the leukoderma around the borders of the lesions on the neck. Since there are healing lesions and developing leukoderma about the elbows and the arms, it is reasonable to believe that the other depigmentation on the body is a direct result of the disease.

DR. DONALD M. PILLSBURY: I think there is no question about the diagnosis on the appearance of the lesions, but I agree with Dr. Gilman that the emaciation and evidence of poor nutrition which this man presents are significant. I think this is a case of lupus erythematosus in which if one does not pay attention to the background one will not get anywhere. I suggest a high vitamin diet. Certainly treatment with gold compounds alone will not produce satisfactory results.

DR. ERICH URBACH (by invitation): I should say that this condition is a subacute exacerbation of discoid lupus erythematosus, and I suggest a porphyrin study, since the man became affected after exposure to the sun. It has been shown that in some such cases porphyrin can be found only in the stool, and by changing the diet I have obtained some good results. I do not say that sensitiveness to light is the cause of lupus erythematosus, but it is one of the factors to be considered.

Rosacea with Keratitis and Corneal Ulceration. Presented by DR. H. P. PARISER (by invitation).

B. J., a white woman aged 51, well developed and not acutely ill, presents an erythematous eruption on the cheeks and about the eyes, associated with erythematous papules, particularly on the nose and chin. There is diffuse scaling of the scalp. The eyelids are reddened and the conjunctivas slightly injected. The left eye shows two minute corneal opacities and the right eye one. A small quantity of pus was expressed from the tonsillar crypts.

The patient had otitis media in 1936. She had aphonia in October 1937, which was cleared by inhalation and sprays. She has had constipation for many years. In November 1937 she had a profuse erythematous papular eruption on both cheeks, the nose and the chin and about the eyes. The eruption has improved partially at times but has flared repeatedly without apparent cause. In December 1938 the left eye became reddened and extremely painful, and there was severe photophobia. Local palliative treatment, roentgen therapy and injections of a gold compound at another institution were without appreciable effect on the skin or on the eye. Early in May 1939 the right eye became somewhat reddened and painful. Blood counts and urinalyses gave normal results, and serologic tests of the blood for syphilis, negative results. Analysis of the gastric contents showed no free hydrochloric acid before or after stimulation with histamine and a considerably diminished total acid content. A culture of material from the corneal lesion showed Staphylococcus albus. Roentgenograms of the chest showed probable old tuberculosis of the upper lobe of the right lung. Roentgenograms of the sinuses showed thickened mucous membrane in the ethmoid and maxillary sinuses. The results of tuberculin tests with old tuberculin, 0.1 cc. of a 1:10,000,000 dilution and a 1:1,000,000 dilution, were negative, but the reaction to 0.00001 mg. of purified protein derivative was positive. The eye was treated with atropine sulfate 1 per cent, 1 drop three times a day, and warm boric acid compresses for twenty minutes four times a day. An oxycholesterol-petrolatum ointment was prescribed for the skin. Internally the patient was given 1 drachm (3.69 cc.) of dilute hydrochloric acid before meals and 1 drachm every hour for three hours after meals; also 2 drachms (7.38 cc.) of calcium gluconate three times a day. Whole milk was given intramuscularly (flare-up?). Liquid petrolatum, sedatives and a soft diet were also prescribed. A tonsillectomy was performed on May 5, with slight improvement of the skin and less injection of the conjunctivas.

DISCUSSION

DR. CARROLL S. WRIGHT: Such cases are interesting from the standpoint of treatment. Two cases stand out particularly in my mind. One patient was sent to me some years ago by an ophthalmologist with the request that if I used roentgen rays I should expose the eye. There was remarkable improvement in the skin, and considerable improvement was noticed in the eyes. Recently I treated a girl aged 14 with this condition; I used extremely small doses of roentgen rays (not over ⅛ skin unit) and did not cover the eyes with lead; the ocular condition became quiescent, and the rosacea disappeared. Of course, I placed the patient on a suitable diet, and Kummerfeld's solution was used locally. (The formula for Kummerfeld's solution is as follows: precipitated sulfur, 3.88 Gm.; pulverized camphor, 0.32 Gm.; pulverized tragacanth, 0.65 Gm.; rose water, 30 cc., and solution of calcium hydroxide, 30 cc.). I think roentgen therapy is indicated for rosacea, together with other therapy.

DR. DONALD M. PILLSBURY: I do not believe that the diagnosis of rosacea has been definitely established. The lesions are definitely papular, which I think suggests the possibility of some tuberculous process. I have treated rosacea in a number of patients with keratitis by exposure of the eyes to roentgen rays. I do not think one takes a great risk. It should be considered that rosacea is often severe, and it is worth taking the slight risk of cataract formation to secure a good result. In a series of cases reported by Dr. Cole of epithelioma in the

ocular region in which the eyes could not be completely protected, there was no instance of cataract in a long series of patients receiving heavy doses of roentgen rays. One should be cautious in most cases, but in this instance the risk is worth taking because it is not great.

DR. JOHN H. STOKES: There is no necessary relation between severe or mild rosacea and so-called rosacea keratitis. Keratitis of identical type occurs in patients in whom one can identify the presence of the flush only in conversation. When the patient first comes into the office the rosacea cannot be seen, but after a few moments' talk the characteristic facial flush appears; this fades out after a short time. It does not necessarily follow that treatment of the rosacea will improve the keratitis or vice versa. I have treated a few patients with roentgen rays and have invariably exposed the eyes. The late Dr. Baer, an ophthalmologist, at first disapproved but subsequently approved my doing so in some of the cases we observed together; so I think it proper to expose the eyes. This type of case is also a good field for testing the nonspecific effect of gold sodium thiosulfate. Some of the patients show extreme sensitiveness to tuberculin, whatever that may mean; but when one uses 2, 3 or 5 mg. doses of gold sodium thiosulfate, one may occasionally, I think, see definite although temporary improvement.

DR. ERICH URBACH (by invitation): At the clinic for diseases of the eye in Vienna, Austria, Dr. Kovacs Muller has used grenz rays extensively, with good results, in cases of this kind of keratitis.

DR. THOMAS BUTTERWORTH, Reading, Pa.: In many pathologic conditions of the ocular regions objections to roentgen irradiation may be overcome by the use of the bare radium plaque. The penetration is much less and in many cases of stubborn lesions on the lids the results are good. For longer exposures I protect the eyeball with a 1 mm. chromium-plated brass shield after anesthetizing the conjunctival sac with 2 per cent solution of phenacaine hydrochloride.

DR. ELMER R. GROSS, Wilmington, Del.: I suggest that milk be given a further trial. Good results in such cases have been obtained at the Wills Hospital (for the eye). The ophthalmologists at that hospital also are using grenz rays.

DR. DONALD M. PILLSBURY: A grenz ray apparatus was secured for the University Hospital, which later gave up its use. There have been many favorable reports in Europe; the use of these rays around the eyes is safe because the penetration is very slight.

Generalized Lupus Erythematosus? Vitamin Deficiency (Pseudopellagra)? Dermatomyositis? Addison's Disease? Presented by DR. A. R. KAUFMAN, Wilkes-Barre, Pa.

A. K., a white man aged 29, presents mahogany pigmentation of the face with moderate cyanosis of the chin. The ears show some evidence of powder lesions from the mines. On the dorsum of each hand, especially around the proximal phalanges, there is pigmentation with atrophy. The right elbow is brawny to the touch and tender. For about one week, in March 1939, the patient noticed swelling of the face for about one day. After this he noticed pigmentation of the face and applied for treatment. Since then the pigmentation has become progressively deeper and the right elbow has started to swell. He has also had weakness and vague pains in various joints.

DISCUSSION

DR. ERICH URBACH (by invitation): The condition looks like pseudopellagra of alcoholic origin. This man eats little, but he has a tendency to drink to excess.

DR. JOHN H. STOKES: I have seen examples of disseminate erythematous lupus in which sudden infiltrations of muscle tissue occurred. They sometimes resolved and sometimes broke down with a discharge of pus. I remember one young man particularly who presented a frightful example of the latter occurrence. He lost a large part of the calf of his leg in one such infiltration followed by

breakdown in the course of disseminate erythematous lupus. I do not know just how one could bring the possible myositis into the diagnosis of alcoholic pseudopellagra. I questioned the patient about trauma, and he said he could not remember any injury. Of course, when I first looked at the man I hoped I was seeing flexure of the biceps due to syphilis, which seems to have occurred in France and nowhere else.

DR. A. R. KAUFMAN, Wilkes-Barre, Pa.: Talbott, Gall, Consolazio and Coombs (*Arch. Int. Med.* **63**:476-496 [March] 1939) described dermatomyositis with scleroderma and calcinosis, and the early picture in the case those authors described seems to agree with that in this case. That is the reason I included that condition among the possible diagnoses.

Exfoliative Dermatitis Treated with Sulfanilamide. Presented by DR. JAMES MURLIN FLOOD (by invitation).

E. P., a white woman aged 60, in fair condition, presents universal erythematous and weeping exfoliative dermatitis. An appendectomy and a cholecystectomy were performed in the summer of 1938. In 1936, three days after receiving a permanent wave (heat method) she noticed unusual scaling of the scalp. This progressed, and the hair began to come out in "handfuls." The scaling continued, involving the ears and neck and gradually the whole body. The last portion of the body to become involved was the face. There have been periodic regressions and exacerbations with no apparent definite cause. The present episode started at the end of March 1939 and has become progressively worse. The itching has become intolerable; by April 20 the patient was hysterical and was receiving large doses of sedatives. One blood count revealed: 4,180,000 erythrocytes and 5,200 leukocytes per cubic millimeter; 78 per cent hemoglobin; 53 per cent polymorphonuclear leukocytes, 30 per cent lymphocytes, 11 per cent monocytes and 6 per cent eosinophils. A blood count after the administration of sulfanilamide showed: 2,500,000 erythrocytes and 11,000 leukocytes per cubic millimeter; 48 per cent hemoglobin; 76 per cent polymorphonuclear leukocytes; 19 per cent lymphocytes; 2 per cent monocytes, and 3 per cent eosinophils. Urinalysis showed a few granular and hyaline casts but no arsenic. Cultures of the urine showed a moderate number of hemolytic staphylococci (Staphylococcus aureus), an occasional colon bacillus, some specimens of Bacillus subtilis and nonhemolytic streptococci. The Kolmer and Kahn reactions of the blood were negative. A roentgenogram of the chest was normal. Histologic examination of the skin showed exfoliative dermatitis. Study of the bone marrow showed it to be normal. The patient was given sulfanilamide as follows: 90 grains (5.7 Gm.) per day for five days; 80 grains (5.17 Gm.) per day for six days; 50 grains (3.24 Gm.) for one day; 30 grains (1.94 Gm.) for one day. It was stopped because of the falling erythrocyte count. Cholesterolized petrolatum and dusting powder were applied locally. At the time of admission paraldehyde and chloral hydrate were given for sedation.

DISCUSSION

DR. E. R. GROSS, Wilmington, Del.: This patient states that she has lived on a farm all her life and has occasionally helped in the fruit picking. The fruit may have been sprayed with arsenate of lead.

DR. DONALD M. PILLSBURY: There is no arsenic in the urine. The hair and nails were not studied. In spite of the severe dermatosis, one cannot demonstrate anything abnormal on examination except the changes in the skin, the urinary infection and the history of a severe nervous upset a few years ago. I do not know whether the nervous upset has any connection with the dermatitis.

A Case for Diagnosis (Pustular Psoriasis? "Id"?). Presented by DR. DONALD M. PILLSBURY.

R. A. D., a white man aged 44, well developed and apparently healthy, presents subsiding scaling erythematous papules on both elbows. There is a superficial

erythematous patch on the right knee and the right pretibial surface. Both hands and feet present sharply outlined patches of small pustules, which are inflammatory at their onset. The pustules show no tendency to extend peripherally. The finger nails are raised at the free border and show some discoloration (probably due to applied medication) and pitting. Near the base they are fairly normal in appearance. General physical examination gave essentially negative results. There are no demonstrable foci of infection. Eleven months ago the patient had a papulosquamous eruption of the elbows, pretibial surface and scalp and recurrent vesiculopustular lesions in sharply marginated patches on the hands and feet. All the finger nails and toe nails have been involved. Scrapings from the lesions (one examination) did not reveal fungi. The intradermal trichophytin test and the staphylococcus ambotoxoid test gave negative results.

DISCUSSION

DR. CARROLL S. WRIGHT: In some 40 cases of psoriasis in which I have tried extensive use of vitamin D, I included a patient similar to this, who was the only one in whose case I felt that I obtained a striking result. This patient had been seen by other dermatologists in different cities and had been treated with sodium cacodylate with temporary improvement, but she continued to relapse. I gave her 300,000 units of vitamin D during about four months. At the end of that time the lesions disappeared, and after eight months she has had no recurrence. One case does not make a series, of course. When I started the vitamin D treatment no other therapy was used.

DR. DONALD M. PILLSBURY: I do not know whether the patient has pustular psoriasis or not, but the picture is suggestive. I have treated 2 patients with this type of eruption with sulfanilamide. One became well; the other did not improve. I feel that in some of these cases staphylococcus ambotoxoid has at times been definitely helpful. If the patient has a positive reaction I give a 1 to 10 dilution of ambotoxoid intracutaneously.

DR. JOHN H. STOKES: Speaking of the ambotoxoid, I think a good many of these patients either have hemolytic staphylococcus infections at the start or acquire them as complications of the process and that they are the part of the condition that responds to the toxoid. The way in which I deal with them is not curative, and I have nothing so definite to offer as Dr. Wright's use of vitamin D, but I think that if the patient can be induced to do the necessary amount of work for about two years, he can gradually bring the infection, if it is such, and its sensitization background under control. In cases in which the process occurred on the heels I have found certain shoe insoles to be contributing factors. When it occurs on the palms one cannot find so satisfactory a cause. I paint the lesions with Castellani's carbolfuchsin paint over and over again. I use sandpaper day after day; when the vesicular phase disappears or is reduced to a minimum, I paint the lesions with a crude coal tar–acetone–collodion paint. If there are any recognizable allergic elements, they should be dealt with, by diet or otherwise, and the nervous state of the patient should have some attention. I have seen hands and feet similarly affected improve for considerable periods after vacations. I remember a young man in whom the condition cleared up and remained well for a long period after a two week trip through the South with the driver of an oil tank. He sat beside him on the box and did nothing but put his feet against the motor, which was as hot as one can imagine. His hands and feet recovered. I have seen patients recover on automobile trips in which they rode with the driver, and I have seen them get worse driving their own cars. I think the persistent mechanical and antiseptic attack on these lesions together with recognition of the fact that they are probably associated with a virus or a hemolytic staphylococcus infection or both, and the attempt to deal with the staphylococcic infection if possible are about as good treatment as I know of at present. I dare say none of the members now is abusing these patients with roentgen rays. Some of them not only do not become better under roentgen ray treatment but become definitely worse.

Book Reviews

The Merck Index. Fifth Edition. Price, $3. Pp. 1060. Rahway, N. J.: Merck & Co., Inc., 1940.

The Merck Index, the first edition of which appeared in 1889, now covers more than 1,000 pages, twice the number of the previous edition, which was published in 1930. It is definitely swelling by accretion. It offers as one of its new features "Chemical, Clinico-Chemical Reactions, Tests and Reagents by the Author's Name" (350 pages). Many of these references have only historical value. However, the volume contains much valuable information.

News and Comment

EXAMINATION BY AMERICAN BOARD OF DERMATOLOGY AND SYPHILOLOGY

The next examination will be given by the American Board of Dermatology and Syphilology at the time of the annual meeting of the American Academy of Dermatology and Syphilology in November 1940 unless sufficient applications have been filed with the secretary before March 1 to make it worth while to hold an examination in New York at the time of the meeting of the American Medical Association, June 10 to 14, 1940.

DEATH OF DR. CHARLES AUGUSTUS SIMPSON

Dr. Charles Augustus Simpson, of Washington, D. C., died suddenly on Dec. 9, 1939.

Directory of Dermatologic Societies *

INTERNATIONAL

Tenth International Congress of Dermatology and Syphilology

Oliver S. Ormsby, President, 25 E. Washington St., Chicago.
Paul A. O'Leary, Secretary-General, 102–2d Ave. S. W., Rochester, Minn.
Place: New York. Time: Summer 1940.

Pan American Medical Association, Section of Dermatology and Syphilology

Elmore B. Tauber, President, 19 W. 7th St., Cincinnati.
Austin W. Cheever, Secretary, 49 Bay State Rd., Boston.

FOREIGN

British Association of Dermatology and Syphilology (Canadian Branch)

L. P. Ereaux, President, 1390 Sherbrooke St. W., Montreal.
F. E. Cormia, Secretary-Treasurer, 2068 Sherbrooke St. W., Montreal.

Royal Society of Medicine, Section of Dermatology

H. W. Barber, President, 7 Devonshire Pl., London, W. 1, England.
Louis Forman, Secretary, 7 Devonshire Pl., London, W. 1, England.

NATIONAL

American Medical Association, Scientific Assembly, Section on Dermatology and Syphilology

John G. Downing, Chairman, 520 Commonwealth Ave., Boston.
C. F. Lehmann, Secretary, 705 E. Houston St., San Antonio, Texas.
Place: New York. Time: June 10-14, 1940.

American Academy of Dermatology and Syphilology

Paul A. O'Leary, President, Mayo Clinic, Rochester, Minn.
Earl D. Osborne, Secretary, 471 Delaware Ave., Buffalo, N. Y.
Place: Philadelphia.

American Board of Dermatology and Syphilology

Howard Fox, President, 140 E. 54th St., New York.
C. Guy Lane, Secretary-Treasurer, 416 Marlborough St., Boston.

American Dermatological Association

Frank C. Knowles, President, 2035 Spruce St., Philadelphia.
Fred D. Weidman, Secretary, University of Pennsylvania, Philadelphia.

Society for Investigative Dermatology

Joseph V. Klauder, President, 1934 Spruce St., Philadelphia.
S. W. Becker, Secretary, University of Chicago, Department of Medicine, Chicago.

* Secretaries of dermatologic societies are requested to furnish the information necessary for the editor to make this list complete and to keep it up to date.

SECTIONAL

Central States Dermatological Association

John C. Kerr, President, 621–14th St., Wheeling, W. Va.
Marvin B. Goldstein, Secretary-Treasurer, Stambaugh Bldg., Youngstown, Ohio.
Place: Buffalo, N. Y. Time: Spring 1940.

Mississippi Valley Dermatological Society

Hamilton Montgomery, President, Mayo Clinic, Rochester, Minn.
Herbert Rattner, Secretary-Treasurer, 25 E. Washington St., Chicago.
Place: Chicago.

New England Dermatological Society

J. Harper Blaisdell, President, 83 Marlborough St., Boston.
Bernard Appel, Secretary, 483 Beacon St., Boston.

Northern New Jersey Dermatological Society

Louis J. B. Le Bel, President, 165 Grant Ave., Nutley.
C. C. Carpenter, Secretary, 38 Waldron Ave., Summit.
Place: Academy of Medicine of Northern New Jersey, Newark. Time: Third Tuesday of March, April, October and December.

Southeastern Dermatological Association

J. R. Allison, Chairman, 1121 Barnwell St., Columbia, S. C.
Howard King, Secretary, 328 Doctors Bldg., Nashville, Tenn.

Southern Medical Association, Section on Dermatology and Syphilology

Howard Hailey, Chairman, 107 Doctors Bldg., Atlanta, Ga.
John H. Lamb, Secretary, 117 N. Broadway, Oklahoma City.

STATE

California Medical Association, Scientific Assembly, Dermatology and Syphilology Section

Nelson Paul Anderson, Chairman, 2007 Wilshire Blvd., Los Angeles.
Julius R. Scholtz, Secretary, 1930 Wilshire Blvd., Los Angeles.

Connecticut State Medical Society, Section on Dermatology

Michael J. Morrisey, Chairman, 18 Asylum St., Hartford.
Harry Bailey, Secretary, 242 Trumbull St., Hartford.

Florida Society of Dermatology and Syphilology

Alan D. Brown, Chairman, 117 W. Duval St., Jacksonville.
Lauren M. Sompayrac, Secretary, 459 St. James Bldg., Jacksonville.

Louisiana Dermatological Society

M. T. Van Studdiford, President, 912 Pere Marquette Bldg., New Orleans.
R. A. Oriol, Secretary-Treasurer, 921 Canal St., New Orleans.

Massachusetts Medical Society, Section on Dermatology and Syphilology

C. Guy Lane, President, 416 Marlborough St., Boston.
J. G. Downing, Secretary, 520 Commonwealth Ave., Boston.

Medical Society of the State of New York, Section on Dermatology and Syphilology

Frank C. Combes, Chairman, 80 W. 40th St., New York.
Rudolph Ruedemann Jr., Secretary, 256 State St., Albany.

MEDICAL SOCIETY OF THE STATE OF PENNSYLVANIA, SECTION ON DERMATOLOGY

Vaughn C. Garner, Chairman, Germantown Professional Bldg., Philadelphia.
Bernhard A. Goldmann, Secretary, 500 Penn Ave., Pittsburgh.

MICHIGAN STATE MEDICAL SOCIETY, SECTION ON DERMATOLOGY AND SYPHILOLOGY

Ruth Herrick, Chairman, 26 Sheldon Ave. S. E., Grand Rapids.
Eugene A. Hand, Secretary, 801 Second National Bank Bldg., Saginaw.

MINNESOTA DERMATOLOGICAL SOCIETY

Carl W. Laymon, President, 345 Medical Arts Bldg., Minneapolis.
F. W. Lynch, Secretary-Treasurer, 317 Lowry Medical Arts Bldg., St. Paul.
Time: First Friday in October, December, February and April.

OKLAHOMA STATE DERMATOLOGICAL SOCIETY

M. M. Wickham, President, Norman.
W. A. Showman, Secretary, 108 W. 6th St., Tulsa.

TEXAS DERMATOLOGICAL SOCIETY

Leslie Smith, President, 109 N. Oregon St., El Paso.
Duncan O. Poth, Secretary, 414 Navarro St., San Antonio.

LOCAL

BALTIMORE-WASHINGTON DERMATOLOGICAL SOCIETY

Walter Teichmann, President, 1726 I St. N. W., Washington, D. C.
Russell J. Fields, Secretary, 1726 I St. N. W., Washington, D. C.
Place: Alternate cities. Time: Third Thursday of each month.

BRONX DERMATOLOGICAL SOCIETY

Marion B. Sulzberger, President, 962 Park Ave., New York.
Henry Silver, Secretary, 290 West End Ave., New York.

BROOKLYN DERMATOLOGICAL SOCIETY

M. J. Cantor, President, 907 St. Marks Ave., Brooklyn.
S. H. Silvers, Secretary, 920 Bushwick Ave., Brooklyn.
Time: Third Monday of each month except June, July, August and September.

BUFFALO-ROCHESTER DERMATOLOGICAL SOCIETY

Richard L. Saunders, President, 333 Linwood Ave., Buffalo.
James W. Jordon, Secretary, 471 Delaware Ave., Buffalo.

CENTRAL NEW YORK DERMATOLOGICAL SOCIETY

Harry D. Parkhurst, President, 264 Genesee St., Utica.
Maxwell C. Snider, Secretary, 106 Oak St., Binghamton.

CHICAGO DERMATOLOGICAL SOCIETY

Edward A. Oliver, President, 55 E. Washington St., Chicago.
Herbert Rattner, Secretary, 25 E. Washington St., Chicago.

CINCINNATI DERMATOLOGICAL SOCIETY

Daniel J. Kindel, President, 1910 Union Central Bldg., Cincinnati.
Lawrence Goldberg, Secretary-Treasurer, Doctors Bldg., Cincinnati.
Place: Cincinnati. Time: First Wednesday of each month, except June, July, August and September.

Cleveland Dermatological Society

C. L. Baskin, President, 159 S. Main St., Akron, Ohio.
Charles G. La Rocco, Secretary, 2060 E. 9th St., Cleveland.

Detroit Dermatological Society

A. R. Woodburne, President, 612 Medical Arts Bldg., Grand Rapids, Mich.
Ruth Herrick, Secretary-Treasurer, 528 Medical Arts Bldg., Grand Rapids, Mich.

Kansas City (Mo.) Dermatological Society

C. C. Dennie, President, 1103 Grand Ave., Kansas City.
Thomas B. Hall, Secretary, 902 Professional Bldg., Kansas City.

Los Angeles Dermatological Society

Chris R. Halloran, President, 1052 W. 6th St., Los Angeles.
Saul S. Robinson, Secretary, 1930 Wilshire Blvd., Los Angeles.
Time: Second Tuesday of each month, October to May, inclusive.

Manhattan Dermatologic Society

George C. Andrews, Chairman, 115 E. 61st St., New York.
Anthony C. Cipollaro, Secretary, 40 E. 61st St., New York.

Montreal Dermatological Society

L. P. Ereaux, President, 1390 Sherbrooke St. W., Montreal, Canada.
Paul Poirier, Secretary, 456 Sherbrooke St. E., Montreal, Canada.

New York Academy of Medicine, Section of Dermatology and Syphilis

Eugene F. Traub, Chairman, 140 E. 54th St., New York.
Louis Tulipan, Secretary, 224 E. 17th St., New York.

New York Dermatological Society

Frank C. Combes, President, 80 W. 40th St., New York.
J. Gardner Hopkins, Secretary-Treasurer, 102 E. 78th St., New York.

Omaha Dermatological Society

Donald J. Wilson, President, 1113 Medical Arts Bldg., Omaha.
Leonard J. Owen, Secretary-Treasurer, 954 Stuart Bldg., Lincoln, Neb.

Philadelphia Dermatological Society

Joseph V. Klauder, Chairman, 1934 Spruce St., Philadelphia.
Herman Beerman, Secretary, 255 S. 17th St., Philadelphia.
Time: Third Friday of each month from September to May, inclusive.

Pittsburgh Dermatological Society

Marvin B. Goldstein, President, Stambaugh Bldg., Youngstown, Ohio.
Charles L. Schmitt, Secretary, Medical Arts Bldg., Pittsburgh.
Time: Third Thursday of every month except July and August.

St. Louis Dermatological Society

Martin F. Engman Jr., President, 3720 Washington Blvd., St. Louis.
Roy L. Kile, Secretary-Treasurer, 3720 Washington Blvd., St. Louis.
Place: Barnard Free Skin and Cancer Hospital. Time: 2 p. m., second Wednesday of each month.

San Francisco Dermatological Society

Merlin T.-R. Maynard, President, San Jose, Calif.
H. V. Allington, Secretary, 3115 Webster St., Oakland, Calif.
Time: Third Friday of February, April, September and November.

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